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Preface.

ARCHIVES OF SURGERY

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STREPTOMYCIN IN THE TREATMENT OF SURGICAL INFECTIONS

Report of Experiences with Its Use

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DETROIT

With the technical assistance of Louie J. Key, R.N., and Lucille Worzniak, M.T.

SURGEONS are called on to treat a number of infections which do not respond to the usual surgical measures or to the forms of chemotherapy that have been available. They are frequently complicated by the presence of intestinal fistulas, intestinal obstruction, urinary obstruction, pieces of dead bone, necrotic fascia or tendon and poor blood supply. Because of these factors and because several types of bacteria are usually present, it is difficult to compare these infections with one another or to classify them for purposes of evaluating therapy. In these respects, they differ significantly from such diseases as pneumococcic pneumonia, meningococcic meningitis, typhoid and gonococcic urethritis, all of which have a simple etiologic agent and run a fairly typical course.

Examples of these infections can be found in any surgical service. They are usually difficult to treat, often persisting for many weeks. For these reasons it is important to search for new methods of treatment and, in spite of the difficulties involved, to attempt to evaluate such new methods.

The new antibiotic, streptomycin, is known from the results of both in vitro and in vivo experiments [1] to be effective against many

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Aided by grants from Merck & Co., Inc., Rahway, N. J., and by the Theodore A. McGraw Fund.

1. Feldman, W. H., and Hinshaw, H. C.: Effects of Streptomycin on Experimental Tuberculosis in Guinea Pigs: A Preliminary Report, Proc. Staff Meet., Mayo Clin. **19**:593-599, 1944. Heilman, F. R.: Streptomycin in the Treatment of Experimental Tularemia, ibid. **19**:553-559, 1944; Streptomycin in the Treatment of

(Footnote continued on next page)

gram-negative and gram-positive bacteria. Since most of the infections under discussion are caused by a mixture of gram-positive and gram-negative organisms, it is important to test the efficacy of streptomycin in their treatment. The purpose of this paper is to present the results of treatment of 55 such infections with streptomycin.

MATERIALS AND METHODS

Streptomycin hydrochloride was supplied by the manufacturer in sealed rubber-capped bottles.[2] The manufacturer's assay value was accepted, and for systemic administration the material was dissolved in sterile isotonic solution of sodium chloride to make concentrations of 10,000 to 100,000 S units[3] per cubic centimeter. The solutions were prepared just before use. Streptomycin was customarily given intramuscularly, either by intermittent injection or as a continuous infusion. In a few instances, it was given intravenously as a continuous infusion in concentrations of 1,000 S units per cubic centimeter of isotonic solution of sodium chloride. For local use in wounds, concentrations from 250 to 1,000 S units per cubic centimeter were employed. The material was usually applied as a slow continuous drip through a small rubber tube incorporated in the dressing. Frequent samples of blood were withdrawn from patients who received streptomycin systemically, and the concentration of streptomycin in the serum was determined by the cup plate method of Stebbins and Robinson.[4] Whenever feasible, the causative organisms were isolated and their in vitro resistance to streptomycin was determined.

RESULTS

Bacteremia.—Nine patients with bacteremia were treated (table 1). In 5 instances, treatment was successful in that the blood stream was sterilized and the patient recovered. In 3 instances treatment failed,

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Experimental Infections with Micro-organisms of the Friedländer Group (Klebsiella), ibid. **20**:33-39, 1945. Jones, D.; Metzger, H. J.; Schatz, A., and Waksman, S. A.: Control of Gram-Negative Bacteria in Experimental Animals by Streptomycin, Science **100**:103-105, 1944. Robinson, H. J.; Smith, D. G., and Graessle, O. E.: Chemotherapeutic Properties of Streptomycin, Proc. Soc. Exper. Biol. & Med. **57**:226-231, 1944. Schatz, A.; Bugie, E., and Waksman, S. A.: Streptomycin, a Substance Exhibiting Antibiotic Activity Against Gram-Positive and Gram-Negative Bacteria, ibid. **55**:66-69, 1944. Schatz, A., and Waksman, S. A.: Effect of Streptomycin and Other Antibiotic Substances upon Mycobacterium tuberculosis and Related Organisms, ibid. **57**:244-248, 1944. Waksman, S. A., and Reilly, H. C.: Bactericidal Action of Antibiotic Substances, J. Infect. Dis. **75**:150-159, 1944. Waksman, S. A.; Bugie, E., and Schatz, A.: Isolation of Antibiotic Substances from Soil Micro-organisms, with Special Reference to Streptothricin and Streptomycin, Proc. Staff Meet., Mayo Clin. **19**:537-548, 1944.

2. Dr. D. F. Robertson, of Merck & Co., Inc., Rahway, N. J., supplied the streptomycin.

3. An Esch. coli, or S, unit of streptomycin is that quantity which when dissolved in 1 cc. of nutrient broth or agar will just suffice to inhibit the growth of a given strain of Escherichia coli. Waksman, S. A.: Standardization of Streptomycin, Science **102**:40-41 (July 13) 1945.

4. Stebbins, R. B., and Robinson, H. J.: A Method for Determination of Streptomycin in Body Fluids, Proc. Soc. Exper. Biol. & Med. **59**:255-257, 1945.

TABLE 1.—*Effects of Streptomycin in Cases of Bacteremia*

Resistance | Serum Level, | Other

TABLE 1.—*Effects of Streptomycin in Cases of Bacteremia*

Patient	Source of Infection	Bacteria Recovered	Resistance in Vitro, Units/Cc.	Dose and Route of Administration	Serum Level, Units per Cc.	Other Therapy	Results
S. W.	Suppurative arthritis	H. influenzae	Not done	50,000 units every 3 hr. intramuscularly for 87 doses; discontinued for 5 days; started again, 250,000 units every 3 hr. intramuscularly for 31 doses	After 1st dose: 1 hr. 0.875; 2 hr. 0.44; 3 hr. 0.44; after 7th dose: 3 hr. 0.44	.....	Blood sterile after 2 doses but joints remained swollen and patient did not improve; blood culture positive 24 hr. after 1st course of therapy ended; blood positive all through 2d course; patient later cured with sulfadiazine
K. L.	Sinusitis	Staph. albus	256	1,000,000 units every 6 hr. intramuscularly for 42 doses; 6,000,000 units daily as continuous intramuscular infusion for 5 days	After 42d dose: 4 hr. 83; during dose of 44th million: about 100.4; 2 hr. after therapy was discontinued: about 112	Penicillin; sulfathiazole	Failure; multiple pulmonary abscesses and cavernous sinus thrombosis
S. V.	Unknown	K. pneumoniae	0.25	1,000,000 units every 6 hr. intramuscularly for 7 doses; 500,000 units every 6 hr. for 16 doses	Not done	Sulfathiazole	Cure
L. L.	Infection of urinary tract	A. aerogenes	8	2,000,000 units per 24 hr.; continuous intravenous infusion for 3 days	15.2 at end of 24 hr. of therapy	.....	Cure
W. T.	Infection of urinary tract and wound	A. aerogenes	2	500,000 units every 6 hr. intramuscularly for 24 doses	After 1st dose: 2 hr. 7; 4 hr. 28; 6 hr. 3.5; after 24th dose: 2 hr. 47.5; 4 hr. 38.3	.....	Patient recovered; blood stream sterilized rapidly, but wound abscess drained on 6th day of therapy; contained alpha hemolytic streptococci, A. aerogenes, Esch. coli; sensitive to 8, 2 and 16 units of streptomycin per cubic centimeter respectively
R. H.	Urinary infection	Esch. coli	Not done	1,000,000 units every 6 hr. intramuscularly for 12 doses; 500,000 units every 6 hr. for 12 doses	After 1st dose: 1 hr. 19.4; 2 hr. 21.4; 4 hr. 31; 6 hr. 20.2; after 6th dose: 6 hr. 23.6; after 16th dose: 6 hr. 13.6	.....	Cure
K. L.	Diabetic gangrene of foot	Esch. coli	32	500,000 units every 6 hr. intramuscularly for 20 doses	.....	.....	Infection of blood stream cured, but other organisms in urine, namely A. aerogenes and Str. viridans, which were extremely resistant, persisted
A. D.	Ruptured appendix	Esch. coli	5	2,000,000 units per 24 hr. as continuous intravenous infusion for 36 hr.; then 1,000,000 units every 6 hr. intramuscularly for 5 doses	After 1st intramuscular dose: 6 hr. 65.6; after 2d intramuscular dose: 1 hr. 77.6; 2 hr. 71.2; 4 hr. 80.8; 6 hr. 65.6; after dose of 5th million: 4 hr. 95.2	.....	Patient died; autopsy showed extensive peritonitis, multiple hepatic abscesses and pyelophlebitis; B. coli recovered from the abscesses
A. G.	Pyelitis	Esch. coli	40	1,000,000 units every 6 hr. intramuscularly for 8 doses; stopped for 24 hr. because of reaction, then 1,000,000 units every 6 hr. for 7 doses	After 1st dose: 6 hr. 40; after 1st dose of second course: 6 hr. 114.5	.....	Patient in critical condition when therapy started; blood promptly sterilized but patient became stuporous 2 hr. after receiving 8th dose of 1,000,000 8 units; blood pressure 85/20; therapy resumed after 24 hr. but patient died after 7,000,000 units; autopsy revealed cirrhosis of liver and pyelonephritis

and in 1 instance (A. G.) the patient died in spite of sterilization of her blood. The cause of death in this case is uncertain. The patient became comatose after receiving 8,000,000 S units of streptomycin over a forty-eight hour period. Therapy was discontinued, and during the ensuing twenty-four hours the condition of the patient improved. Therapy was started again, but the patient gradually failed, and she died after receiving an additional 7,000,000 S units over forty-two hours. Autopsy revealed cirrhosis of the liver and pyelonephritis.

An analysis of these cases reveals that although streptomycin sterilizes the blood promptly it does not sterilize walled-off collections of pus (patients W. T. and A. D.), even though a serum concentration of streptomycin is present which, on the basis of in vitro tests, is more than adequate to inhibit growth of the organisms in the abscess. The following case illustrates this point.

W. T., a white man, 41 years of age, had had the left kidney removed a number of years ago. Shortly before he consulted us a stone became impacted in the right ureter, and on March 9, 1945 he was examined by means of a cystoscope and a catheter was passed to the right renal pelvis. The day of cystoscopy chills and fever developed and the patient became extremely ill. During the next few days, in spite of penicillin therapy and an adequate urinary output, he failed to improve. On March 16 the stone was removed surgically. Chills and fever persisted; the man became critically ill and on March 21, and again on March 22, Aerobacter aerogenes was recovered from his blood stream. Streptomycin therapy was initiated on March 22 in doses of 500,000 S units intramuscularly every six hours and continued until March 28, a total of 12,000,000 S units being given. In vitro the organism was inhibited by 2 units of streptomycin per cubic centimeter. The concentration of streptomycin in the patient's serum was as follows:

	Time After Dose, Hr.	Units per Cc. of Serum
First dose	2	7.0
	4	28.0
	6	3.5
Second dose	2	47.5
	4	38.3

After one day of treatment, the temperature, which had varied from 97 to 104 F., leveled off at 100 to 100.5 F., and subsequent blood cultures were sterile. On March 27, the sixth day of therapy, a small abscess in the wound was drained. The temperature fell to normal the following day and remained so. Streptomycin was discontinued on March 28. The following organisms were recovered from the wound abscess:

	In Vitro Sensitivity to Streptomycin, Units per Cc.
Alpha hemolytic streptococci	8
Aerobacter aerogenes	2
Escherichia coli	16

In spite of the fact that all these organisms were inhibited in vitro by concentrations of streptomycin less than the patient presumably had in his serum during most of his therapy, they were not killed but persisted and caused fever until the abscess was drained.

Peritonitis.—Streptomycin was administered to 12 patients with peritonitis, caused in 5 instances by perforation of the appendix, in 6 by rupture of a peptic ulcer and in 1 by a perforation of a carcinoma of the cecum. The results of therapy in these cases (table 2) are difficult to assess. First, peritonitis is an unpredictable disease. Some patients who appear critically ill recover with surprising rapidity, while others, who at first do not seem as sick, may die or recover only after a protracted illness. Second, the bacterial flora in peritonitis is usually complex, and often all the offending organisms are not recovered by the usual methods of culture. Third, some of the patients in cases reported in this paper had penicillin or sulfadiazine in addition to streptomycin, because the surgeons in charge were reluctant to withhold any treatment which might be of benefit to a patient who was critically ill.

Because of the reasons listed, it is unwise to conclude a great deal from this small group. It is apparent, however, that in these cases streptomycin had no spectacular effect. The patients with peritonitis resulting from perforation of the appendix followed the course that one was accustomed to observe before the advent of chemotherapy. One patient with generalized peritonitis who had been sick for three days recovered after nineteen days. Another, who had been ill for only two days, recovered after six days. In this instance, however, the peritonitis was rather mild. Pus which was aspirated from the peritoneum yielded only Staphylococcus albus, diphtheroid bacilli and nonhemolytic streptococci. In a third patient, who was also treated conservatively, a pelvic abscess formed but the patient finally recovered, after twenty-four days. In a fourth patient (A. D.), who was reported in the group with septicemia, pylephlebitis with hepatic abscess developed and the patient finally died. It should be observed that in this instance streptomycin therapy was not instituted until the patient was almost moribund. The pylephlebitis and hepatic abscess were probably already present. None of these patients were operated on. The fifth patient, a girl 14 years of age, had an appendectomy after the appendix had perforated. In spite of treatment with streptomycin an infection of the wound and a pelvic abscess developed, but the patient recovered after about three weeks. Similarly, the patients in whom peritonitis was the result of perforation of a peptic ulcer did not recover spectacularly under treatment. The patient whose peritonitis was due to perforation of a carcinoma of the cecum had been ill for ten months and was admitted to the hospital with a large intra-abdominal abscess. A fecal fistula followed drainage of the abscess. Although the patient's general condition was so poor that further intervention was not warranted, an ileotransverse colostomy was done. It was discovered at this operation that the patient had a plastic peritonitis. In spite of vigorous strepto-

TABLE 2.—*Effects of Streptomycin in Cases of Peritonitis*

Patient	Source of Infection	Bacteria Recovered	Resistance in Vitro, Units/Cc.	Dose and Route of Administration	Serum Level, Units per Cc.	Other Therapy	Results
E. B.	Appendicitis; appendectomy	A. aerogenes Esch. coli Alpha hemolytic streptococci	2 5 —	1,000,000 units every 6 hr. intramuscularly for 26 doses	After 1st dose: 2 hr. 36.6; 4 hr. 22.5; 6 hr. 17.4; after 7th dose: 2 hr. 48; 4 hr. 25; 6 hr. 20.4; after 11th dose: 2 hr. 48.4; 4 hr. 42; 6 hr. 24.4	None	Recovery after 3 wk.; pelvic abscess developed which subsided without drainage and wound infection containing A. aerogenes resistant to 5 units per cc.; alpha streptococci resistant to 16 units per cc.; B. melaninogenicus and unidentified gram-negative rod
H. M.	Appendicitis; no operation	Esch. coli Ps. aeruginosa A. aerogenes	6 41 5	250,000 units every 6 hr. intramuscularly for 43 doses	.....	Penicillin 15,000 units every 3 hr. intramuscularly for 56 doses	Recovery after 24 days; pelvic abscess developed, which subsided spontaneously
T. D.	Appendicitis; no operation	Esch. coli Gram-negative rods, unidentified Bacteroides melaninogenicus; anaerobic gram-positive coccus; anaerobic streptococci	4 62	1,000,000 units every 4 hr. for 19 doses, then every 6 hr. for 4 doses intramuscularly	.....	Penicillin	Recovery after 19 days
C. B.	Appendicitis; no operation	Staph. albus; diphtheroid; gamma streptococci	..	1,000,000 units every 6 hr. for 20 doses intramuscularly	.....	Penicillin 15,000 units every 3 hr.	Recovery; temperature elevated 6 days
A. D.	Appendicitis; no operation	Esch. coli	5	2,000,000 units per 24 hr. continuous intravenous infusion for 1½ days, then 1,000,000 units every 6 hr. for 5 doses	After 1st dose intramuscularly; 6 hr. 65.6; after 2d dose intramuscularly: 1 hr. 77.6; 2 hr. 71.2; 4 hr. 80.8; 6 hr. 65.6; after 5th dose intramuscularly: 4 hr. 95.2	.....	Death; autopsy showed extensive peritonitis, pylephlebitis and liver abscess

A. O.	Peptic ulcer perforated	Alpha hemolytic streptococci	..	1,000,000 units every 6 hr. intramuscularly for 16 doses	.....	Penicillin 15,000 units every 3 hr.	Temperature elevated for 7 days; recovery
E. P.	Perforated ulcer	Anaerobic coccus; alpha hemolytic streptococci	..	1,000,000 units every 6 hr. intramuscularly for 17 doses	.....	Penicillin 15,000 units every 3 hr.	Temperature elevated for 5 days
W. M.	Perforated ulcer	Alpha hemolytic streptococci	..	1,000,000 units every 6 hr. for 29 doses	.....	Penicillin 15,000 units every 3 hr.	Temperature elevated for 7 days
F. G.	Perforated ulcer	B. subtilis; alpha hemolytic streptococci; anaerobic diphtheroid; anaerobic gram-positive coccus	0.25	1,000,000 units every 6 hr. for 25 doses intramuscularly	.....	Penicillin 20,000 units every 2 hr. intramuscularly	Wound infection developed from which were recovered: yeast resistant to more than 256 units per cc. alpha streptococci, anaerobic diphtheroid, Staph. albus resistant to 0.5 unit per cc.; rash and drug fever; afebrile on 9th postoperative day, 3 days after drug discontinued
F. Mc.	Perforated ulcer	No growth	..	1,000,000 units every 6 hr. intramuscularly for 13 doses	.....	Penicillin 15,000 units intramuscularly every 3 hr.	Temperature normal in 3 days
P. T.	Perforated ulcer	No culture	..	500,000 units every 6 hr. intramuscularly for 17 doses	.....	.....	Temperature normal after 5 days
B. K.	Perforated carcinoma of the cecum	Staph. aureus; alpha hemolytic streptococci; Esch. coli; anaerobic diphtheroid; anaerobic gram-positive rod with spores, not identified	8	1,000,000 units intraperitoneally at operation; 1,000,000 units every 12 hr. intramuscularly for 26 doses	.....	.....	No benefit; wound infection developed; death

mycin therapy, 1,000,000 S units in the abdomen at operation and 1,000,000 intramuscularly every twelve hours for twenty-six doses, the patient failed to improve and the wound became infected. Culture of material from the wound yielded a hemolytic Staphylococcus aureus, an alpha hemolytic streptococcus, Esch. coli, an anaerobic coccus and an unidentified anaerobic gram-positive sporulating rod. The staphylococcus was sensitive to 8 units of streptomycin per cubic centimeter and the colon bacillus to 8 units also. Although this patient was perhaps not suitable for treatment, it is in such circumstances that help is needed.

It has been shown that streptomycin can be recovered from peritoneal exudate after systemic administration.[5] If the organisms causing peritonitis are susceptible to streptomycin, such treatment should be beneficial. Apparently the reason that treatment with streptomycin was not attended by spectacular success is that peritonitis is usually a mixed infection and a number of the bacteria involved are resistant to streptomycin. Among the most important of the resistant organisms are the non-spore-forming anaerobes.

Infections of Soft Tissues.—In this group there were 3 patients with pelvic abscess due to salpingitis or perforation of the bowel and 3 patients with wounds of the back or buttocks, in 1 of whom the wound followed injection of liver extract into the gluteal muscles, in 1 it was a shotgun wound of the back and in 1 a large undermined area of the lower part of the back and buttocks, which had started as a decubitus ulcer. There were, in addition, 6 patients with the following infections: hepatic abscess secondary to pelvic inflammatory disease, infected nephrectomy wound of flank, infected wound of the abdominal wall following ileotransverse colostomy, abscess of the breast, abscess of subcutaneous tissue of the thigh and cellulitis of subcutaneous tissue of the thigh. In only 1 of the cases can it be established that streptomycin played an important role in curing the infection. Failure in the other cases can be attributed to the presence of anaerobic non-spore-forming organisms, resistant aerobes or an inadequate dose of streptomycin.

The following case illustrates the type of response that occurred in this group.

M. W., a 39 year old Negro woman, had an exploratory laparotomy on March 24, 1945 and was found to have diffuse peritonitis due to pelvic inflammatory disease. The wound was closed without drainage. On April 1, 1945 an abscess presented in the lower aspect of the wound and was drained. A large quantity of foul yellow pus continued to escape from the abscess, which extended into the pelvis. Alpha and beta hemolytic streptococci, Bacteroides melaninogenicus,

5. Buggs, C. W.; Pilling, M. A.; Bronstein, B., and Hirshfeld, J. W.: The Absorption, Distribution and Excretion of Streptomycin in Man, J. Clin. Investigation **25**:94-102, 1946.

an anaerobic gram-positive coccus and anaerobic diphtheroids were recovered from the pus. Streptomycin therapy was started on April 4, the patient receiving 500,000 S units intramuscularly every six hours and 500,000 units in 1,000 cc. of isotonic solution of sodium chloride dripped constantly in the wound during twenty-four hours. On April 7 the intramuscular dose was increased to 1,000,000 S units every six hours. On April 11 the drip in the wound was discontinued, and by April 13 the intramuscular therapy was stopped because of severe toxic symptoms in the form of fever, generalized myalgia and painful swelling of the shoulder and wrist joints. Six hours after the last intramuscular dose of streptomycin, the serum concentration was 173 S units per cubic centimeter. Although the wound had improved a great deal, several observers agreed that the improvement was no more than would have occurred without chemotherapy. The alpha and beta hemolytic streptococci had been eliminated, but the anaerobes remained unchanged. In addition, Staph. aureus and an aerobic diphtheroid had appeared. The wound finally closed, and the patient was discharged, only to return three weeks later with a recurrent abscess.

The experience with this group of cases indicates that streptomycin is not effective against Bacteroides melaninogenicus and many of the anaerobic cocci which play such a prominent part in infections originating from the intestine or female genital organs. Unfortunately, many of the soft tissue infections which harbor gram-negative organisms such as Esch. coli, which are susceptible to streptomycin, also contain these resistant anaerobes. Until an antibiotic is found which will at least inhibit these organisms, the use of streptomycin will produce only partial improvement. If some means is found to control the organisms that are resistant to streptomycin, the use of a combination of the two agents should be extremely effective.

Infections of the Urinary Tract.—Streptomycin was given to 13 patients with infections of the urinary tract. In 7 of these patients therapy eliminated the infecting organisms from the urine, while in 6 the urine was not sterilized. In 5 of the 6 cases with unsatisfactory outcomes failure was due to the presence of organisms which were resistant at the time therapy was instituted, while in 1 case the organisms appeared to be extremely susceptible when therapy was started but, for some reason, acquired resistance rapidly and were not eliminated. After parenteral administration a large proportion of the streptomycin is excreted in the urine,[5] and it is logical to expect that streptomycin will be effective in the treatment of urinary infections provided the organisms are susceptible. Many of these infections are mixed, and, since some of the organisms are apt to be resistant, streptomycin often will have to be used in combination with other agents in order to insure success.

Infections of Bone.—There were only 2 patients in this group.

One was a 38 year old Negro woman in whom painful swelling of the right thigh developed four months before she was admitted to the hospital. This had occurred shortly after a confinement. On admission to the hospital, April 17, 1945,

she was found to have an extensive soft tissue abscess of the right thigh, which apparently had its source in the femur. The abscess was drained, and culture of the pus yielded a beta hemolytic streptococcus and an anaerobic coccus. For a time the patient improved, but after a short time she became febrile again and on May 4 streptomycin was started, 1,000,000 S units intramuscularly every six hours. Streptomycin had to be discontinued after twenty-one doses because of nausea and vomiting and pain at the sites of injection. Penicillin therapy was substituted. Two days later a new lot of streptomycin was obtained, and the drug was started again in doses of 1,000,000 S units every six hours. At this time, culture of material from the wound yielded Staph. aureus, diphtheroids, Pseudomonas aeruginosa, an alpha hemolytic streptococcus and an anaerobic coccus; all the aerobes were resistant to more than 256 units of streptomycin per cubic centimeter of culture medium. The resistance of the anaerobes to streptomycin was not determined. The drug was discontinued after four days because of the severe local irritation at the sites of injections, the resistance of the aerobes and the failure of the anaerobes to disappear. Although this patient received only a short course of treatment, streptomycin seemed to have no effect. The anaerobes persisted, and the wound became contaminated with resistant aerobes during therapy.

The other patient was a man of 70 years, who had a chronic ulcer over the internal malleolus of the left ankle which finally involved the joint. While the organisms recovered from the wound varied somewhat from time to time, Ps. aeruginosa, Bacteroides melaninogenicus and a gram-positive anaerobic coccus seemed to be constantly present. These organisms persisted throughout eighteen days of treatment, during which time the patient received 500,000 S units of streptomycin intramuscularly every six hours and 1,000,000 S units in 1,000 cc. of isotonic solution of sodium chloride locally over each twenty-four hour period.

Failure in these 2 cases does not indicate that streptomycin will be of no value in osteomyelitis caused by susceptible organisms. It does indicate, however, that it will probably fail when Bacteroides melaninogenicus and other anaerobic bacteria are present. Furthermore, it indicates that during treatment open wounds may become contaminated with other bacteria which either are resistant or acquire resistance rapidly.

Granulating Surfaces.—Four patients were studied who had sloughing or granulating wounds resulting from third degree burns or avulsion of skin. The drug was applied locally as a wet dressing in concentrations of 200 to 500 S units per cubic centimeter. All the patients did well in that the granulating areas became red and healthy and grafts took well. Interestingly, there was no significant change in the bacterial flora, most of the organisms which were present at the start of therapy still being present when it was discontinued. During the period of therapy, their resistance to streptomycin increased remarkably. It is difficult to evaluate this small group of patients. They might have done just as well with moist dressings of isotonic solution of sodium chloride.

Diabetic Gangrene.—In this group of 4 patients, there were 2 for whom streptomycin therapy was classed as failure. In 1 case, that of

a patient with an infected amputation stump and renal failure, streptomycin was started only a few days before death and obviously did not have a fair trial. The other failure occurred in a patient with an infected foot. Streptomycin was employed both as a local drip of 1,000 S units per cubic centimeter and as an intramuscular injection in doses of 500,000 S units every six hours. The infecting organisms were as follows:

	In Vitro Resistance to Streptomycin, Units per Cc.
Ps. aeruginosa	128
Gram-negative rod (unidentified)	96
A. aerogenes	56
Alpha hemolytic streptococci	80
Anaerobic gram-positive coccus	Not done

The serum level was 36 S units per cubic centimeter six hours after a dose on the second day of therapy. During four days of treatment, the foot became worse, so that amputation was finally done. Culture at this time yielded:

	In Vitro Resistance to Streptomycin, Units per Cc.
Ps. aeruginosa	256
Unidentified gram-negative rod	80
Alpha hemolytic streptococcus	56

The other 2 patients showed remarkable improvement of their infection under local streptomycin treatment. In 1 case, that of an infected amputation stump, the concentration of streptomycin employed locally was 200 S units per cubic centimeter, while in the other, a case of an infected foot, it was 2,000 S units per cubic centimeter.

It was not possible to correlate the bacteriologic observations with the clinical improvement.

Miscellaneous.—A number of patients were treated whose infections could not be classified in any of the preceding groups. Their diseases are as follows:

	No. of Patients
Miliary tuberculosis	1
Tuberculous meningitis	1
Acute pulmonary moniliasis	1
Chronic prostatitis	1
Urethral fistula	1
Friedländer's pneumonia	1
Chronic cholangitis	1

S. B., the patient with miliary tuberculosis, was admitted to the hospital on May 11, with no symptoms other than temperatures as high as 104 F., for three weeks prior to admission. Physical examination was entirely noncontributory, but roentgenologic examination revealed a fine mottling of both pulmonary fields suggestive of miliary tuberculosis. The temperature ranged from 100 to 104 F. By May 28 fine rales had appeared in both pulmonary fields. Administration of

streptomycin was started on May 25 in doses of 1,000,000 S units intramuscularly every six hours and was continued for one hundred and twelve doses. Serum levels were as follows:

	Hours After dose	Units
After 1,000,000 S units.....	2	26.5
	4	15.2
After 16,000,000 S units.....	2	31.0
	4	19.0
	6	16.8
After 48,000,000 S units.....	2	26.4
	5	13.6
After 77,000,000 S units.....	2	26.7
After 78,000,000 S units.....	1	32.7

During treatment there were no perceptible changes in the patient's course. Some time after treatment was stopped he died, and the diagnosis of miliary tuberculosis was established at autopsy.

The patient with tuberculous meningitis was a boy 4 years old, who was almost moribund when streptomycin therapy was initiated. He received 750,000 S units intramuscularly every six hours for a total of eight doses. He also received 10,000 S units intrathecally. Six hours after the first dose the serum concentration was 31.8 units per cubic centimeter; six hours after the third dose it was 171 units, and at the time of death, five and one-fourth hours after the last dose, it was over 300 units.

Streptomycin obviously did not have a fair trial in this case. Whether the high concentration of streptomycin contributed to his death is not known. The case does illustrate that streptomycin may accumulate in a critically ill patient and emphasizes the need for caution in the treatment of such patients.

The case of acute pulmonary moniliasis deserves little comment. The organism was completely resistant to streptomycin, its in vitro sensitivity being greater than 250 units per cubic centimeter. Treatment had no perceptible effect on the course of the disease.

No benefit was obtained in the case of chronic prostatitis. Although there was considerable variation in the bacteria which were recovered, probably due to contamination from the urethra, an alpha hemolytic streptococcus with a sensitivity of 4 to 16 units per cubic centimeter appeared to be the causative organism. Treatment consisted in administration of 500,000 S units intramuscularly every six hours. After twenty-five doses, drug fever developed and therapy had to be discontinued. Unfortunately, no serum levels were obtained, and it is possible that failure was due to an inadequate dose.

The patient with a urethral fistula had had a suprapubic cystotomy in 1931, for an unknown reason. He had remained well until October 1944, when a purulent urethral discharge developed. The cystotomy wound opened, and a perineal abscess formed. After the abscess was drained, a urethral fistula appeared.

The fistula failed to heal, the wounds were indolent and the urine was thick and foul. Culture of materials from the bladder yielded the following organisms:

	Resistance to Streptomycin, Units per Cc.
Staph. aureus	0.45
Beta hemolytic streptococcus	1.90
P. vulgaris	0.45
Ps. aeruginosa	14.30
Bacteroides melaninogenicus	Not done
Anaerobic diphtheroid	Not done
Anaerobic gram-negative bacillus	Not done

Treatment with streptomycin consisted in emptying the bladder, then in instilling 100 cc. of a solution containing 200 S units of streptomycin per cubic centimeter into the bladder every four to six hours. The patient retained the material for several hours by plugging the cystostomy opening, after which he voided. Four days of therapy was sufficient to cause pronounced improvement; cultures at this time yielded Proteus vulgaris, Staph. aureus, a diphtheroid and anaerobes which could not be isolated. Improvement continued, and both wounds healed promptly.

The case of chronic cholangitis deserves little comment, since the dose was too small to be effective. This patient was one of the first to be treated, and he received only 10,000 S units every two hours and then, after a few days, 50,000 S units every two hours. There was no effect on his course or on the bacterial flora of the drainage from the common bile duct. The organisms were sensitive to small concentrations of streptomycin, and failure is probably explained by the inadequate dose.

Although streptomycin failed in the patient with Friedländer's pneumonia, this case cannot be accepted as indicating in any way the place of streptomycin in the treatment of this condition. The patient, who was 58 years old, was admitted to the hospital primarily because of a cerebral vascular accident. During examination it was discovered that he had extensive pneumonia. Although Klebsiella pneumoniae was the predominant organism in the sputum, many other organisms were present in the sputum.

	Sensitivity to Streptomycin, Units per Cc.
K. pneumoniae	0.25
Alpha hemolytic streptococci	Not done
Staph. aureus	2
M. aurantiacus	1
Gram-negative bacilli	4
M. candidus	1
Esch. coli	5
Bacteroides melaninogenicus	Not done
Anaerobic gram-negative bacilli	Not done
Anaerobic diphtheroid	Not done
Anaerobic gram-positive coccus	Not done

The patient received 1,000,000 S units intramuscularly every six hours. Serum levels following the first dose were: 10.1 units per cubic centimeter at two hours; 11 at four hours and 7.3 at six hours. He died after receiving 7,000,000 S units.

Streptomycin was used prophylactically in an attempt to prevent peritonitis in 2 patients in whom the peritoneum was soiled during operative procedures. In 1 case, that of a patient with ulcerative colitis in whom the colon was torn, no infection occurred. In the other case, that of a patient with intestinal obstruction in whom the bowel was torn and extensive soiling occurred, infection did occur, but she recovered, the convalescence being far smoother than was anticipated. It is difficult to say how much benefit was obtained from therapy in these cases, but certainly the results indicate the need for further trial.

TOXIC SYMPTOMS

Streptomycin was administered to 56 patients, the cases of 4 not being included in this paper because of insufficient data. The discrepancy between the number of cases reported in the paper (55) and the figures just given is due to the inclusion of 3 patients under two categories. Of the 56 patients who received streptomycin, 12 exhibited definite toxic symptoms and 1 manifested symptoms which may have been due to streptomycin.

The toxic symptoms were fever, rash, weakness, myalgia, arthralgia, arthritis, nausea and vomiting. The 1 fatal case, in which symptoms may have been due to streptomycin (A. G.), was discussed in the bacteremia group. The toxic symptoms were usually severe enough to warrant cessation of therapy. Whether they were due to impurities which can be eliminated as the process of manufacture is improved or to streptomycin per se is not known. In addition to these toxic symptoms, most patients complained of considerable pain and persistent soreness at the sites of intramuscular injections. In many instances these areas exhibited induration, which persisted for several days.

COMMENT

The patients whose cases are presented in this paper were selected for treatment in order to test the value of streptomycin. Some patients were chosen because they had lesions which were probably hopeless, while others were treated because they had infections which, while not customarily fatal lesions, were those for which there was no satisfactory treatment. Still others were included in hopes that streptomycin might prove to be better than the current treatment. It is for these reasons that the cases are so varied. Although neither the total experience nor the number of cases in any one group is large, we believe that it is possible to draw certain conclusions from this experience.

First, it is fairly clear that streptomycin is capable of sterilizing the blood stream in short order provided the infecting organisms are susceptible to a serum concentration of the drug that can safely be maintained. If a larger experience proves this statement to be true, it

means that streptomycin will be a valuable agent in the rare cases of septicemia due to Esch. coli, A. aerogenes, Ps. aeruginosa and other gram-negative bacilli.

Second, streptomycin, since it is excreted in high concentrations in the urine, is able to sterilize urine that is infected with susceptible organisms. Used in conjunction with other agents, streptomycin should make it possible to cure more patients with mixed infections of the urinary tract than it has been possible to do in the past.

The apparent lack of response to therapy of the patients with peritonitis and infections of the soft tissues was disappointing. This is probably due to the fact that in most instances these were mixed infections, in which some of the organisms were resistant. The nonsporulating anaerobes seemed to be the chief offenders in this regard. In spite of the failure of streptomycin to render these lesions sterile, its use is still rational for the elimination of some of the organisms and should make it easier for the body to combat those which remain.

Streptomycin seems to follow the rules that hold for the sulfonamide drugs and penicillin in that it does not sterilize walled-off collections of pus or wounds harboring dead tissue and foreign bodies. Its use in such instances is not wise, because many bacteria seem to acquire resistance to streptomycin rapidly. It is wiser, therefore, by adequate surgical treatment to render the conditions as suitable for its action as possible before streptomycin therapy is initated.

Streptomycin therapy at present is accompanied with a high incidence of toxic symptoms. Whether these can be reduced as the process of manufacture is improved is not known.

SUMMARY

Fifty-six patients with various types of infection were treated with streptomycin. Manifestation of toxicity occurred in 12 of these patients.

In patients with bacteremia or septicemia, streptomycin sterilizes the blood stream promptly provided the organisms are susceptible to its action.

Streptomycin does not sterilize walled-off collections of pus, even though the organisms involved are susceptible to its action.

Owing to the high concentration in which streptomycin is excreted in the urine, it is a valuable agent for the treatment of infections of the urinary tract, provided the organisms are susceptible to its action.

The results of treatment of patients with peritonitis and various types of infections of the soft tissues were disappointing. Most of these infections were caused by a mixture of several kinds of bacteria, and failure in the majority of instances can be attributed to the presence of resistant organisms; the most prominent group of resistant organisms appeared to be the nonsporulating anaerobes.

PHYSIOLOGIC CONSIDERATIONS IN THE CARE OF PATIENTS WITH VARICOSE VEINS

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THE current shortage of labor has increased the number of patients who seek treatment for varicose veins or their complications. The symptoms, which previously had been negligible or at least tolerable, have become important after long hours of work. If these patients are to be able to work in comfort, they must have more treatment than the casual bandage, injection or ligation. So it seems worth while to present, somewhat dogmatically, a system of management which applies to the large majority of the simpler cases. It lays no claim to newness or fundamental originality but is founded on the practices developed at the Outpatient Department of the University of California Medical School. This treatment of ulcers has been tested in the Outpatient Department of the John Sealy Hospital at Galveston, Tex.

PHYSIOLOGY AND PATHOLOGY

The chief features of all varicose conditions, considered from a physiologic point of view, are valvular incompetence, raised venous pressure and edema.

Probably the commonest primary defect is congenital inadequacy in one or more pairs of venous valves at the upper end of the long saphenous system. The transmission to the saphenous system of a pressure wave, on coughing or straining, shows that the valves in the femoral vein just above the saphenous opening are commonly faulty (Adams [1]). Occasionally (1 per cent of all cases of Ochsner and Mahorner [2]) a valve may be at fault where the lesser saphenous vein pierces the fascia to join the popliteal vein. The familial tendency [3] of these disorders strongly

1. Adams, J. C.: Etiological Factors in Varicose Veins of the Lower Extremities, Surg., Gynec. & Obst. **69**:717 (Dec.) 1939.

2. Ochsner, A., and Mahorner, H.: Varicose Veins, St. Louis, C. V. Mosby Company, 1939.

3. de Takáts, G., and Quint, H.: The Injection Treatment of Varicose Veins, Surg., Gynec. & Obst. **50**:545 (March) 1930.

suggests congenital weakness. But in some patients, varicose veins must be ascribed to destruction of valves during thrombophlebitis, superficial or deep, of the leg and thigh. Because damage is widespread, such patients are difficult to treat satisfactorily.

With regard to the common and probably congenital type, it seems likely that mild incompetence during the years prior to adolescence may alter the function thereafter. Generalized venous breakdown may be accelerated or precipitated by pelvic congestion (uterine enlargement at puberty or pregnancy, constipation, pelvic inflammatory disease, fibroids or other conditions), by prolonged standing or by occupations which involve repeated straining, with raised intra-abdominal tension.

As the upper valves fail, the column of blood sustained by the lower valves becomes longer and therefore heavier, and they, in turn, give way. The increased tension within the larger veins usually produces a thickening of their muscular coat so that they feel straight, firm and thick. Such vessels extirpated from young subjects have been reported as arteries after casual pathologic examination. Prolonged increase of pressure on the smaller vessels tends to produce distention, thinning and tortuosity of the veins—the typical varix.[4]

In such veins the course of the blood is demonstrably downward, toward the lower part of the calf. Here the blood enters the deep veins by the vessels perforating the fascia and ascends, only to flow back via the saphenofemoral junction or a perforating vessel in the thigh whose directing valve is incompentent. Thus, reverse flow is established, with raised venous pressure and venous stagnation.

The stagnant anoxia and raised venous pressure combine to upset the balance of turnover of the tissue fluid and produce edema. The chronic stretching of the connective tissue by excess tissue fluid or the chronic anoxia from stagnation of the tissue fluid or perhaps both are followed by formation of fibrous tissue and discoloration of the skin.

I. VARICOSE VEINS WITHOUT COMPLICATIONS

History.—The familial incidence of varicose veins, the amount of disability they have caused and the effects of treatment should be investigated. The rate of development of signs and symptoms, the responses to treatment and occupational changes, the effects of pregnancy or abdominal diseases and the probable expectation of life of the patient, obtained from an examination of personal, family and occupational history, should be used to evaluate the prognosis of the varicose condition and the probability of recurrence after treatment. Often it will be found that the treatment of choice and the advice given with respect to occupa-

4. Epstein, S.: Ueber die Structur normaler und ectatischer Venen, Virchows Arch. f. path. Anat. **108**:239, 1887.

tion may be determined by the fact that a particular patient has a short expectation of life and his varices have a tendency to progress only slowly, in contrast with the patient who has a long expectation of life and whose varices have a tendency to progress rapidly. Evidence should be sought which might indicate extra caution in the use of intravenous treatments and also the psychologic and the physical factors which might determine the advisability of surgical procedure. Inquiry should be made as to itching, tenderness, aching, heaviness, swelling or tiredness, particularly in the calves and ankles. Examination and history should be weighed to evaluate the adequacy of the arterial circulation below the knee, since arterial inadequacy makes treatment by injection or operation more hazardous. Particular attention should be paid to the exact time, nature, quality and success of previous treatments and to a history which might be interpreted as thrombophlebitis. In this connection, if the condition of the patient required his being hospitalized or confined absolutely to bed for a period of ten days or longer, the thrombophlebitis was almost certainly in the deep femoral system. The history of superficial saphenous thrombophlebitis shows variation and confusion.

Examination.—The size and apparent tension of all visible veins in the lower extremity should be noted and a search made for varices in the vulva, the lower part of the abdomen and the gluteus muscles. Whether visible or not, the long saphenous vein should be palpated and traced throughout its course by the transmission of a percussion wave along it (Schwartz test). When it is stroked empty and allowed to fill from above, convincing evidence should be obtained that the saphenous vein is conveying blood downward (reverse flow). The procedure should be applied also to as many branches as possible. The thickness of its wall should be noted. The arterial circulation should be evaluated by the temperature of the feet, their color when dependent, the qualities of the skin, the palpation of the posterior tibial and dorsalis pedis arteries and such other tests as may seem helpful. At the same time the feet should be examined for deformities or orthostatic defects which might be producing pain or tiredness.

It is seldom that treatment of the veins will affect complaints above the knee. Any pain or discomfort above the knee should instigate a diligent search for causes other than varicose veins. Usually the exceptions are small superficial veins on the outer thigh or the vulva. The results of treatment of vulval varices during the child-bearing years are unsatisfactory (Homans [5]), but injections early in pregnancy often give temporary relief and have not been found to complicate delivery. A

5. Homans, J.: Circulatory Diseases of the Extremities, New York, The Macmillan Company, 1939.

further, but obvious, exception is the pain arising from superficial saphenous thrombophlebitis. The exquisite pain of this condition usually is promptly relieved by ligation high in the saphenous system. The presence of ulceration, dermatitis, edema, pronounced telangiectasia or pigmentation should be noted at this time; their bearing on treatment will be discussed later. Careful examination should be made for cracks between the toes, macerated thickened white skin, abnormal proliferation of epithelium around the legs and other evidences of fungus diseases.

Tourniquet Tests.—While the patient lies on his back, his foot is elevated and a narrow rubber tourniquet applied tightly just below the head of the fibula; then he is brought immediately to his feet. Normal filling of the veins below this tourniquet by blood flowing through the capillaries will take from twenty-five seconds to a minute or longer. It is more rapid in the lower part of the leg and depends largely on the temperature of the feet. By contrast, in the absence of any unusual condition, such as an arteriovenous aneurysm, filling of these veins in less than twenty-five seconds is from above and indicates either that the tourniquet is not sufficiently tight or else that the perforating veins, which normally carry blood from the superficial external and internal saphenous systems to the deeper veins of the leg, are carrying their blood in the reverse direction as a result of valvular incompetence. It is of great importance that the status of these valves be evaluated surely, because the patient with incompetent communicating valves below the knee can at best be rehabilitated only partially; he must be taught to exercise constant care and to expect more or less trouble during the rest of his life.

Whether the perforated veins below the knee are competent or not, the same tourniquet test is repeated with the tourniquet a little above the knee. Here again, tightness of the tourniquet is of great importance. If the hamstring tendons are such that there is doubt as to whether the veins are properly occluded, a pad of cotton placed under the tourniquet over the saphenous vein will assure the occlusion. As the patient stands, rapid filling of the vein indicates reversed flow in a vein perforating the fascia distal to the tourniquet; if there has been no incompetence below the knee, it may be inferred that one is dealing with incompetence at the place where the short saphenous vein perforates the fascia into the popliteal space.

A tight tourniquet should next be placed high up on the thigh, below the saphenofemoral opening, and the test repeated. Rapid filling in this case suggests a major incompetence somewhere in the length of the thigh, and this has been shown to occur most commonly about 16 cm. above the knee. Finally, while the patient is standing the tourniquet at the top of the thigh is released, and rapid or immediate filling indicates

incompetence of the valves of the long saphenofemoral opening. The large majority of all patients with varices or symptoms due to venous back pressure have gross incompetence at the saphenofemoral valve; of these, a large proportion reveal some degree of incompetence in the thigh, although this often is difficult to evaluate.

In the evaluation and localization of incompetent valves in perforating vessels in the thigh, the comparative tourniquet test of Mahorner and Ochsner [6] is often valuable and should be studied.

Treatment.—The aim of all treatments of varicose veins is the elimination of back pressure on the capillaries, which gives rise to all the symptoms and disabilities, and since this back pressure originates from the fact that there is somewhere, usually at the saphenofemoral opening, an incompetently guarded communication between superficial and deep systems of the veins so that blood tends to flow backward and down the superficial veins, the logical treatment is the elimination of all the perforating vessels whose valves are incompetent. The only way in which one can be sure of achieving this is to ligate each of the affected perforating veins and excise part of the vein at the time. This procedure is relatively straightforward in the case of perforation at the saphenofemoral opening and it is spoken of as "high saphenous ligation." It may be performed with the patient under local infiltration anesthesia, but the operation should not be regarded as an office procedure (see recent discussion by Atlas [7]) unless it is performed by a surgeon with considerable experience in an office unusually well staffed and equipped. Inquiry tends to show that the more experience a surgeon acquires, the less he is inclined to regard this as an office procedure.

High saphenous ligation has been adequately described many times,[8] but it is still necessary to emphasize, first, that the dangers and the sources of error be kept in mind, and, second, that the operation will not give uniformly good results unless enough of the femoral vein is thoroughly exposed to make sure that no tributaries are formed above the point at which the saphenous vein has been tied. Any such tributary should be tied and cut and a sufficient length removed. The stump of the long saphenous vein should be tied as closely as possible to the femoral vein and a transfixed suture placed immediately distal to the tie. Two inches (5 cm.) of the saphenous vein and any branches which may arise within these 2 inches should be excised, the vein and

6. Mahorner, H. R., and Ochsner, A.: A New Test for Evaluating Circulation in the Venous System of the Lower Extremity Affected by Varicosities, Arch. Surg. **33**:479 (Sept.) 1936.

7. Atlas, L. N.: Hazards Connected with the Treatment of Varicose Veins, Surg., Gynec. & Obst. **77**:136 (Aug.) 1943.

8. Tavel: Behandlung der Varicen durch die Ligatur und die künstliche Thrombose, Cor.-Bl. f. schweiz. Aerzte **34**:617, 1904.

branches having been ligated distally before excision. At this stage, most operators inject distally into the main trunk of the saphenous vein a sclerosing solution. The wisdom of this procedure has been questioned by Atlas [7] and will be discussed later.

This operation should be followed by active movements of the legs to the fullest extent that they can be tolerated and the patient sent back to work within a few days. The amount of temporary disability from this operation is determined largely by the extent of reaction to the injection of sclerosing solution.

A large proportion [9] of patients so treated return some months or years later with recurrence of the varicose veins. Many times these recurrent lesions are due to technical imperfections in the operation, such as ligation too low or failure to visualize the femoral vein and therefore failure to ligate all its branches at the upper end. In such cases, anastomotic channels may be established around the site of ligation and carry blood into varicose veins. Yet a considerable proportion of the recurrences are in patients in whom the original surgical operation appears to have been technically satisfactory and in whom symptoms return without evidence of recurrence of incompetence in the region of the groin. On repetition of the test outlined, it is shown that the recurrence is due to a back flow from the femoral vein through the perforating vessels in the thigh into the saphenous system and recanalization of the saphenous system. The logical procedure here would be to locate and tie the perforating vessel in the thigh. This is often not one vessel but several; their locations are difficult to determine, and, in fact, systematic anatomic description of this part of the saphenous system and its connections rests entirely on the recent work of Sherman [9]; it is reasonable to suppose that further work in confirming Sherman's findings will give additional information as to the constancy and the inconstancy of the location of these vessels. In view of the difficulty of locating these particular vessels, Sherman has advocated and used with great success a revival of the Mayo stripping procedure.

Sherman's procedure is designed to interrupt the perforating vessels which communicate between the deep (femoral) and the saphenous system of the veins; the removal of the long saphenous vein is incidental to this end. Because of the common recurrence after simple high ligation, Sherman advised that the stripping operation be done at the same time as the high ligation whenever there is evidence of incompetent midthigh perforators. Stripping might sometimes be done for prophylactic reasons, even when this evidence is not obtainable. Hemorrhage, which might be expected to accompany this operation, is controlled by injection of a sclerosing solution. Three to 5 cc. of solution of monoethanol-

9. Sherman, R. S.: Varicose Veins: Anatomic Findings and an Operative Procedure Based upon Them, Ann. Surg. **120**:772 (Nov.) 1944.

amine oleate is injected into the distal stump of the great saphenous vein during the operation, and the vein is then nicked and inspected to make sure that it does not bleed. The procedure is designed to explore the pattern taken by the saphenous vein and to avulse all parts of it which might communicate with the deep system. The technical details are adequately described in the original article. Local infiltration anesthesia is not satisfactory; spinal or general anesthesia are preferable.

Reaction to the trauma of passing the vein stripper down the length of the thigh and part of the leg is surprisingly small, and, in fact, these patients usually complain less of soreness than those who have had a simple high ligation with retrograde injection. It may be that removal of the vein and the sclerosing solution that it contains prevents the persistent inflammation which results otherwise. These patients usually are encouraged to use their legs as much as possible; they are sent home on the day following the operation and are back at work in ten days or so. This early return to activity is advisable so as to minimize the possibility of thrombosis with embolism and to promote rapid healing. It is important also since these patients are more cooperative if they are assured that they will be able to return to work almost immediately.

The immediate results of this procedure are extremely satisfactory to the patient and appear to achieve what is desired, as far as can be measured by available methods for testing. The logic of this method leads one to suppose that the results may be permanent in the large majority of patients (that is to say, patients in whom there is no incompetence of the short saphenous vein or of the veins below the knee), but, naturally, a further report on Sherman's early cases must be awaited before this treatment can be offered as a permanent cure.

Many authors, feeling that a stripping operation is too radical a procedure for most cases, advocate a simultaneous high and low ligation of the internal saphenous vein. In many patients so treated, severe varices and their complications continue to develop.

So far, no mention has been made of treatment by injection. Injection of sclerosing solution often will give complete relief of symptoms but usually is followed by recanalization and recurrence, sometimes within twelve months and usually within three years, although occasionally one meets patients who have been treated satisfactorily by injection seven or eight years prior to the recurrence. Because of its temporary nature, it seems that the sclerosing treatment is useful only in certain limited ways. These may be listed as follows: (1) as a treatment of trifling varices for cosmetic reasons; (2) as a procedure in cases in which arterial insufficiency, short expectation of life or other general reasons contraindicate surgical intervention; (3) as a temporary measure when it is necessary to defer operation; (4) as a treatment when surgical operation is refused; (5) as a procedure during pregnancy; (6) as a

supplement to surgical treatment, both before the stripping operation and afterward, to obliterate any distended veins which do not disappear after operation, and (7) as a measure in cases in which incompetent perforating veins below the knee limit the success of operative procedure. The short saphenous perforator, when incompetent, may be satisfactorily ligated when necessary where it perforates the fascia. Many varices of the short saphenous system are referable to its connections with the long saphenous system.

Incompetent perforating veins below the knee cannot as a rule be satisfactorily ligated, because they usually are multiple and of uncertain location. The prognosis of the patient with this condition is poor, and he must be educated to remain constantly on guard. His long saphenous vein should be ligated or stripped if there is clear evidence that it is involved. Into every accessible vein in his calf injections should be made carefully, and he should frequently be examined for veins which require injection. Whenever edema is detected, it should be eliminated either by rest in bed or by a tight pressure tape. When edema has been eliminated, its return should be prevented either by a tight heavyweight elastic stocking or by a heavy, well fitted canvas gaiter. Extreme care must be taken to prevent trauma and fungus infections, as these are the principal precipitating causes of varicose ulcers, particularly with incompetent valves in the perforating veins below the knee.

II. COMPLICATIONS OF VARICOSE VEINS

The outstanding complications of varicose veins are (1) dermatitis or eczema, (2) edema, (3) varicose ulcer and (4) thrombophlebitis.

Dermatitis.—Itching is a common symptom among patients with varicose veins. The complaint varies from mild occasional itching to severe weeping dermatitis complicated by scratching, or a dry, exfoliative type of dermatitis with considerable fibrosis of skin and subcutaneous tissues. The itching may be due in part to the rapid migration of fluid from one part of the tissue to another, particularly in the skin where there are nerve endings which characteristically give rise to this sensation. This may be compared with the itching along the advancing edge of the lesion of giant urticaria, but it is probable that the greater part of the itching in patients with varicose veins is associated with fungus infection. The fungus tends to thrive on the moist surface of edematous tissue; the low oxygen tension which probably obtains as a joint result of the reflux of blood and the stagnation of tissue fluid also favors fungus infection. Attempts to establish the role of the fungus in varicose dermatitis are not yet conclusive; however, careful control of fungus infection often leads to the rapid cessation of itching and the regression of the physical signs of the dermatitis, whereas when a localized fungus infec-

tion is permitted to spread intolerable itching occurs. The cutaneous lesions often become secondarily infected with pyogenic organisms. For these reasons, the prime treatment of varicose dermatitis consists in control of the edema which allows the fungus to thrive. Measures directed toward the destruction of the fungus itself are helpful; considerable study has been given to the relationship between fungus infection and various vascular disorders of the extremities by Thompson,[10] whose work bears importantly on the topics discussed in this paper.

Moderate varicose dermatitis usually responds promptly to high ligation of the saphenous vein if there is no evidence of other venous incompetence, but, in view of the likelihood that the infection will invade the site of operation, it is probably wiser to defer surgical treatment until the dermatitis is controlled. The importance of postponing radical treatment was clearly apparent during the care of 2 patients with ulcers and severe obstinate lymphedema. Apparently this lymphedema had developed as the result of low grade infection in the groin. This infection occurred shortly after high saphenous ligation had been performed without previous control of obvious infection below the knee. The chain of cause and effect is not established by these cases, but they constitute a warning.

Occasionally, if the edema is not pronounced, varicose dermatitis will respond to the simple application of 5 or 10 per cent silver nitrate in 50 per cent alcohol to the entire surface involved and to the interdigital spaces and the crevices around the nails. Yet again, success may be had by the application of a tight inelastic support, of the nature to be described for the treatment of varicose edema, though in certain instances the warmth and the moisture which accumulate beneath such a dressing, by encouraging the multiplication of fungi, produce more harm than the reduction of the edema warrants. In cases in which it is economically possible, a few days in bed with the legs elevated will reduce edema. The itching usually can be controlled and the weeping dried by the frequent application of a turkish towel wrung out of a hot strong solution of magnesium sulfate. The immediate relief of itching is essential for effective treatment. In a refractory case, the judicious use of dilute phenol preparations locally or barbiturates internally should be tried once or twice early in the treatment. In the cases of the most obstinate dermatitis, with considerable weeping and little edema or when the response to the treatment of edema does not clear up the dermatitis, mild roentgen therapy once a week for three weeks or so is helpful.

In any case, when the dermatitis has been alleviated the leg must be thoroughly supported until successful operative measures control the

10. Thompson, K. W.: Studies on the Relationship of Dermatomycosis to Ulceration and Gangrene of the Extremities, Yale J. Biol. & Med. **16**:665 (July) 1944.

edema more permanently. If the edema has been eliminated completely, the most satisfactory way to continue its control is by the use of an adequate elastic stocking or a carefully designed gaiter.

Edema.—In all patients with varicose veins, the control of edema is paramount. Pitting edema of recent origin if due to varicose veins can be eliminated rapidly by rest in bed, with the feet elevated. In like circumstances, tight bandaging will produce the same results with less economic loss but usually with more discomfort. This procedure is based on the work of Nobl,[11] Pondroff,[12] and others. Since the effective use of the tight bandage depends on the proper balance of a number of technical details, its application is here described.

Application of Pressure Bandage.—First, the leg, foot and nails should be scrupulously cleaned by scrubbing with soap and water and then washed in alcohol and ether. The whole leg from knee to toe, including all cracks, crevices and surfaces of all lesions, should be painted with silver nitrate solution as a prophylactic measure against fungi. To provide proper spreading, this salt should be in 50 per cent alcohol and be 5, 10 or 15 per cent silver nitrate. The weaker solutions seem to be adequate if there is no recognizable evidence of active fungus infection. The stronger solutions appear to be more effective in the control of fungus. Silver nitrate produces irritation in a significant proportion of patients; the application should not be repeated in these, but attempts should be made to control the fungus by some other fungicide.

Next, the leg should be given two coats of compound tincture of benzoin, time being allowed for drying between applications. Care should be taken to prevent this solution from running in between the toes, because of its unpleasant stickiness.

The same area is next carefully covered with a layer of cotton sheet wadding, every precaution being used to avoid wrinkles.

Two pieces of ½ inch (1.27 cm.) rubber sponge are cut to fit the legs from end to end of the fibula, each being about 4 to 6 inches (10 to 15 cm.) wide, according to the size of the leg. The sponge rubber should be soft and all edges carefully beveled at a 45 to 30 degree angle. These strips of rubber are placed outside the wadding on either side of the leg and temporarily held in place with ½ inch adhesive tape. If they are previously wrapped in cellophane, they may be used repeatedly.

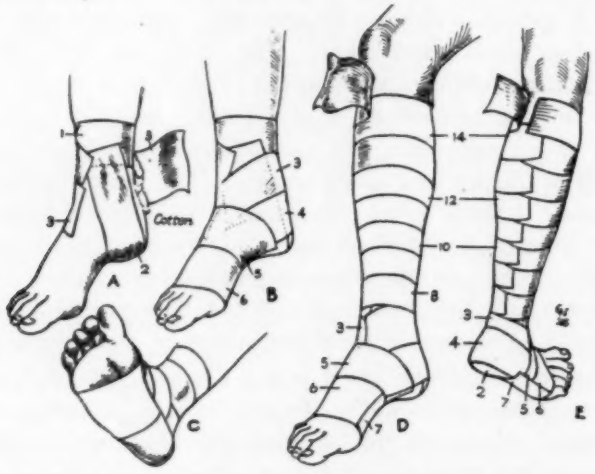
Next, a 4 inch gauze bandage is applied from the metatarsophalangeal joint over the sponges up to the knee, going around tightly up and down

11. Nobl, G.: Druckbehandlung von Stauungsgeschwüren, Wien. klin. Wchnschr. **37**:644, 1924.

12. Pondorff, cited by De Gaetano, L.: La cura ambulatoria delle ulceri varicose, Gazz. med. lomb. **84**:99, 1925.

the leg as often as may be necessary to insure that the sponges are well compressed, that all the cotton is covered and that there are no obvious kinks or pinches. Extra wadding should be placed over the tendo Achillis.

Adhesive tape should be applied in such a way as to encase the leg rigidly and to compress the rubber sponge to its maximum extent. Usually it is advisable to design the taping in such a way that at every place there are at least two thicknesses of tape. Although the types of compression and support desired cannot be achieved with the so-called elastic tapes, the water-proof type of tape is so inelastic that it invariably wrinkles and causes abrasions. For this reason, the old style, rough surface adhesive tape should be used.



Details of application of adhesive tape. Strips are applied in the numbered order as indicated in the text. If edema is evident, the tape should be applied as tightly as possible.

The following details (see figure) of application seem to have helped in preventing or minimizing the discomforts and abrasions which this procedure usually produces sooner or later:

1. A strip of 3 inch tape (7.6 cm.) is applied as tightly as it can be stretched all the way around the leg just above the malleoli. The tightness of the whole taping procedure is of prime importance.

2. A stirrup of 3 inch tape is applied tightly, anchored to the first tape, passed over the internal malleolus and the plantar surface of the heel near the back and up over the external malleolus and anchored again to the first piece of tape.

3. One or two pieces of 3 inch tape are applied tightly, centered over the tendo Achillis overlapping each other passing over the malleoli and also over the back of the heel and extending down to ground level, with the ends crossing on the dorsal surface of the foot.

4. A tape is centered over the dorsal surface of the foot, passing transversely and finishing under the plantar surface. This tape is necessary to prevent bulging edema or to reduce edema of the dorsum of the foot, and for this reason it should be placed as low as is practicable. But, on the other hand, if it interferes in any way with the movement of the metatarsophalangeal joint it will produce bruising, discomfort and abrasions. For additional comfort, the sole, or rather the ends of tape which are under it, may be covered with a single piece of 3 or 4 inch (7.6 or 10 cm.) adhesive tape.

5. Another piece of 3 inch adhesive tape is put directly over the first, and from there on a series of flat tapes is placed around the leg up to the top, with slight overlapping. Unless the bulge of the calf is exceptionally clear and prominent, it is important that the upper inch of tape be anchored directly to the benzoin-coated skin and not to the cotton. This prevents the dressing from slipping down the conical leg and failing to give support.

Before the dressing is considered complete, the tension of the sponge should be explored with the thumb in order that additional tight tapes may be applied wherever the sponge feels soft. This usually is necessary in the region of the ankle. It is particularly important to warn a patient when he is to wear this type of dressing that it involves some discomfort. Discomfort from the extreme degree of tightness with which it has been put on will wear off within an hour or so and will be negligible the following day; on the other hand, irritation, itching and discomfort may develop because the skin is covered and wrinkles may abrade it. Generally speaking, the patient will tolerate this first dressing for a week, but a clear understanding should be had that if the dressing is intolerable it must not be removed but that he will return to the physician for redressing. Flesh colored tape, which has proved perfectly satisfactory, is somewhat less unsightly than white. The liberal application of powder over the surface of the dressing half an hour after it is complete will prevent the adhesive from picking up fluff and other particles. If the patient is to wear such dressings for a long time, as is necessary with many patients with chronic ulcers or lymphedema, it is worth while to advise him that by rubbing the outside of the dressing with a block of paraffin he may render it sufficiently waterproof to enable him to take a quick shower.

Further Care.—At the end of a week, the dressing may be removed by the physician. The leg should be cleaned with soap, alcohol and ether; abrasions should be touched up with silver nitrate or other coagulant antiseptics and protected with gauze or, better, with adhesive tape applied directly to the surface of the skin. The dressing should be put on again as before. The second and subsequent dressings usually can be worn for two weeks, depending on the resistance of the skin of the patient

and on his temperament. The decision as to whether to repeat or to omit the application of silver nitrate every time or to change antiseptics must be an individual consideration. Thymol iodide seems to be helpful in some cases in which the skin is easily irritated. (Care must be taken not to use this compound with or immediately after a mercury antiseptic.)

In the application of pressure dressings care must be taken to be sure that there is adequate arterial supply. This involves not only the palpation of the dorsalis pedis and the posterior tibial arteries but also a general evaluation of the patient. In the case of a young person with normal arterial supply and considerable edema, the whole dressing should be applied with all the strength of which the ordinary physician is capable. In proportion as there is less edema, more gentleness should be used. The edges of the sponge if improperly beveled will give rise to blistering; in any case it is wise, on successive dressings, to move the sponges slightly in order to prevent repeated trauma.

When the edema has been eliminated by a few weeks of this pressure therapy, the leg of the patient should be measured carefully for a well fitting elastic stocking. This should be made of heaviest one way stretch lastex material available and so designed as to fit tightly at all points. A stocking with a seam down the back is significantly more satisfactory than a woven one. (Stockings with seams are at present unavailable because of regulations by the War Production Board.) Such a stocking, if the fit is imperfect, can be adjusted by an intelligent patient or a stocking saleswoman. If there is edema at the time the stocking first is fitted, there will be a tendency for rings or so-called "rubber tires" to develop around the lower part of the leg. These are unsightly, uncomfortable and conducive to damage of the skin.

Such a tight stocking should be put on over an ordinary silk or rayon stocking, both because this facilitates cleanliness and because the stocking can be drawn on more easily over silk than over skin. Support of this nature will generally be adequate until such time as it is possible to eradicate the cause of edema. If this is not possible, such a stocking will be adequate for from four to eight months, after which time it should be renewed; sometimes it is necessary to spend a week or two reducing the edema before such a replacement.

In the extremely heavy type of leg with much fibrosis, and particularly in the presence of lymphedema, an elastic stocking sometimes is inadequate for proper control. Control may then be obtained by a carefully fitted canvas gaiter or a legging incorporating stay ribs and made to lace up tightly. The patient should be instructed carefully with respect to the importance of putting this on before getting out of bed in the morning, tightening it firmly and evenly and keeping it on all day.

A delicate skin or a normal skin with considerable fungus infection is likely to break down into weeping dermatitis during the prolonged

course of the adhesive tape treatment. For that reason, every precaution should be taken to hurry the treatment and to control invading organisms. It is striking how rapidly a weeping, itching and abraded skin will recover once the edema is eliminated and the leg is supported by a proper stocking in the daytime and treated with a mildly antiseptic powder at night.

Great stress is laid on the elimination of edema, not merely because it is unsightly and is an invitation to pathogenic organisms but because it is the ground on which the successful varicose ulcer grows. Edema is the principal cause of varicose dermatitis, and if present for a long time it tends to give rise to pigmentation and fibrous tissue, which not only is undesirable in itself but makes more difficult the healing of chance abrasions or ulcers. Incidentally, the fibrosis resulting from long-standing edema makes the treatment of the edema itself more difficult; however, the hard, brawny fibrotic skin and subcutaneous tissue of a person with edema of long duration may be considerably softened by the judicious application of the procedures outlined before.

It is a wise rule to take every precaution against the first appearance of edema, to attack and eradicate it whenever it is found and to keep up the struggle against it even when treatment seems unsuccessful. It is often worth while to measure carefully the ankle of a patient with varicose veins without edema and to repeat the measurement frequently in order that incipient edema may be detected.

Varicose Ulcer.—The true varicose ulcer heals spontaneously and rapidly in the absence of edema, venous back flow or vascular insufficiency.

It is well known that the majority of varicose ulcers will heal fairly rapidly with rest in bed and elevation of the foot; if they do not do so, it is generally due to arterial insufficiency, anemia, syphilis or some other complicating factor. Such ulcers as will heal by rest and elevation may be healed with equal or greater rapidity and with considerable economic advantage by relieving them of the edema by the pressure bandage method.

The surface of the ulcer (as well as the rest of the leg) is painted with silver nitrate, and a piece of adhesive tape large enough to adhere to ½ inch (1.27 cm.) of skin around the ulcer is placed directly over the surface of the ulcer immediately after a sterile coagulum is formed by the silver nitrate. A large beveled rubber sponge is placed directly over this tape, and cotton, gauze and adhesive pressure bandage are applied as mentioned before. Wherever the ulcer may be, the pressure bandage should extend from the metatarsophalangeal joint to well above the site of the ulcer; it usually is best to carry it right up to the knee.

An untreated inflamed ulcer, particularly if it is directly over subcutaneous bone, often is exquisitely painful. The patient with such an ulcer will rarely accept the pain involved in application of the pressure

bandages. The patient should be heavily dosed with codeine and acetylsalicylic acid, and a dressing of weak phenol should be applied directly over the ulcer for half to one hour before any attempt is made to apply the dressing. The patient should be given every assurance that the treatment will rapidly eliminate the edema which is the cause of the pain and the tenderness, and he should be provided with enough codeine to insure freedom from pain for two or three days and with a proper sedative for two good nights. These patients will rarely mind the second and never the subsequent dressings. They are considerably relieved of pain within two days of the application of the first dressing and are so well pleased with this relief that they usually are less disturbed by the various discomforts than are the patients who have not had considerable pain previously.

After the ulcer is healed and dry, it is important that care be not immediately discontinued but that adequate support be given until the new epithelium is toughened and until the cause of the edema is otherwise controlled. Any method of supportive control of edema is useful, but the most satisfactory is the elastic stocking. In the case of a small ulcer on a leg with minimal fibrosis and edema, a two way stretch lastex stocking gives adequate support and is more comfortable and less unsightly than the heavier type. When the ulcer has been a large one or is on an indurated leg or one with poor arterial supply, a heavy stocking should be used and for the first four or six weeks after removal of the pressure tape the newly healed area should be covered with a beveled rubber sponge. During these weeks, all patients should be instructed to attend carefully to the hygiene of the feet at least twice a day; the stocking should be worn whenever the patient is not recumbent, and a midday rest with elevation of the leg and removal of the stocking should be advised. During this time the patient should be informed that neglect of this care of the healing area or failure to give continued care to control or eliminate the varicose state will almost certainly result in a recurrence of the ulcer.

Thrombophlebitis.—For practical convenience in the consideration of varicose veins, thrombophlebitis may be regarded in three categories, though they are not completely separable.

Low Grade Superficial Thrombophlebitis: First for consideration is low grade superficial thrombophlebitis, which may or may not migrate a little. Patients with varicose veins occasionally will complain of soreness or bruising where small areas of thrombophlebitis develop and involve an inch (2.5 cm.) or so of the superficial venous system. This rarely gives pain enough to require treatment, but it is necessary to make sure that the complaint is due neither to thromboangiitis obliterans (Buerger's disease), if it is occurring in the lower part of the extremities, nor to the onset of a rapid and progressive thrombophlebitis. Once

the diagnosis is made with certainty, the patient may be reassured that the lesion of which he complains will not become worse but will gradually resolve itself, though he may have other such lesions elsewhere. He should be told also that thrombophlebitis is beneficial to a certain degree and that it does for him exactly what would be done by an injection of sclerosing solution at that point.

Progressive Superficial Thrombophlebitis: Extensive superficial varices occasionally start an area of rapidly progressive superficial thrombophlebitis of the saphenous system. This happens frequently during pregnancy, when the lessening of physical activity tends to slow the flow of blood and perhaps thereby contributes to the thrombotic tendencies already associated with the damage to the veins. It has been suggested also that there may be chemical reasons which make thrombosis more apt to occur in pregnancy. Such a thrombosis commonly starts between 6 inches (15 cm.) below and 6 inches above the knee on the inner side in one of the branches of the long saphenous vein, usually the more superficial one. It spreads rapidly, at the rate of from 1 to 6 inches (2.5 to 15 cm.) per day. The region is exquisitely tender and painful. It is hot and red, and it may be accompaned with a slight fever and other signs of infection. When this condition occurs in the subfascial branch of the saphenous vein around the level of the knee or slightly above and when it is not seen early in its course, it is sometimes difficult to differentiate from deep thrombophlebitis. Both the immediate and the remote prognosis and also the proper treatment demand that this differentiation be promptly and accurately made. It rests to some extent on careful palpation to determine the exact location of the tissues involved.

When untreated, superficial femoral thrombophlebitis generally progresses up to the saphenofemoral opening but rarely invades the femoral system, nor does embolus commonly occur. For this reason it is allowable to use the conservative and the conventional methods of treatment, namely, rest in bed, elevation, codeine, antipyretics and either hot or cold packs, whichever offers the more relief. Physiologic consideration, no less than common clinical observation, seems to suggest that cold applications, though usually offering more relief, tend to prolong the course of the disease and to delay resolution.

If this condition is seen while the thrombophlebitis is still clinically below the midthigh, it is advisable to ligate the saphenous vein at the saphenous opening promptly and completely. This gives immediate relief of pain and rapid resolution of the disease and is anticipating a surgical procedure which would be called for later in any case. This has been done successfully as late as the seventh month of pregnancy. No reports are at hand of such intervention after the thrombophlebitis has approached the region of the upper thigh; but since there is no great

hazard from superficial thrombophlebitis and since the pain can to a large extent be controlled by rest, elevation and codeine, it is probably unjustifiable to attempt this procedure near an inflamed area.

The disability from acute superficial thrombophlebitis lasts anywhere from a few days to three weeks or more, depending on the extent of the process and the temperament of the patient. Sometimes it can be treated on a purely ambulatory basis, and again it may require time spent in bed; generally, although the limb is more comfortable when elevated, the pain is not severe enough to preclude movement, except in patients who are temperamentally intolerant of pain. This superficial thrombophlebitis, then, is an unpleasant and usually an unimportant incident in the course of the progressive deterioration of the limb with varicose veins; McPheeters,[13] however, gave a grave prognosis and regarded this condition as the forerunner of an ulcer.

Deep Femoral Thrombophlebitis: Deep femoral thrombophlebitis, by contrast, is a serious matter, involving a real hazard to life from embolus and a probability of some degree of permanent disability. This condition, known also as milk leg, white leg, phlegmasia alba dolens or marble leg, is well recognized as occurring about the tenth day after a sudden cessation of physical activity. It commonly follows hospitalization for childbirth, abdominal operation, fractures and typhoid. It may also occur after relatively trifling injuries of the foot in which the foot is rested and favored either by the patient's own will or by immobilization of it with the help of adhesive tape.

In the more fortunate patients, deep tenderness will be found in the region of the interosseous membrane in the middle of the leg; this signalizes the beginning of the thrombosis in the deep veins of that part. Ordinarily it is difficult to differentiate this from various and sundry muscle aches and tendernesses which may arise from immobilization or from the discomfort of awkward positions of the patient in bed or under anesthesia. At the other extreme, the condition may be heralded by a fatal pulmonary embolus or by any degree of embolic phenomenon in the lung, even a subclinical infarct which may be discovered at autopsy. However, in the majority of cases, pain, enormous swelling of the whole thigh and leg and signs of infection are the first recognized signs of deep thrombophlebitis and embolic phenomena may or may not follow. After the diagnosis is established, the hazard of a fatal embolus must be recognized. Some of the treatments advocated will be listed here without critical discussion, since it seems that early diagnosis and painstaking care are of greater importance in determining the immediate prognosis than is the particular treatment used: (1) immediate ligation of the femoral vein below the junction of the profunda femoris vein and removal of the clot by aspiration; (2) sympathetic block of the region

13. McPheeters, H. O.: Varicose Veins, ed. 2, Philadelphia, F. A. Davis Company, 1930.

by paravertebral injection of procaine hydrochloride; (3) rest and cold packs, accompanied with elevation, and (4) use of heparin given intravenously or of dicoumarin (3, 3'-methylene-bis-[4-hydroxycoumarin]) given by mouth with a view to increasing coagulation time and thus lessening the risk of extension of the clot, thereby diminishing the chance of embolus.

At this time it should be emphasized that the incidence of this disaster is generally associated with immobilization, and in conditions involving rest in bed, whether concerned with varicose veins or not, every possible effort should be made to keep the legs active from the earliest possible moment and to get the patient walking as soon as possible.

The discussion of deep femoral thrombophlebitis is included in this consideration of varicose veins because of the poor prognosis of its varicose sequelae. As long as the deep femoral circulation is completely blocked, the superficial saphenous circulation remains as the only venous return from the leg. The increased load is likely to stretch the veins and produce a relative or functional incompetence of the valves of the long saphenous system, and if this continues too long the back pressure which results produces permanent varicose veins.

It has not been possible to collect adequate information as to the proportion of all patients with deep thrombophlebitis in whom varicose veins subsequently develop, but a history of thrombophlebitis is fairly common in a clinic devoted to varicose veins, particularly in patients who show obstinate varicose conditions with much edema, with valvular incompetence below the knee and with prominently bulging calves. A patient with this syndrome, that is, much edema, incompetent veins below the knee, a prominently bulging calf and a history of thrombophlebitis, or with any considerable part of the syndrome will have more or less disability with respect to that leg for the rest of his life; for this reason, every effort should be made to follow the patient who has had a deep thrombosis with all possible care in order to try to forestall or delay the development of this disability. A number of suggestions to be discussed are obvious points which merit attention, but there is not any clearcut evidence as to whether the patients receiving good care do better in this respect than those who are completely neglected.

The thrombophlebitic patient should be kept in bed with the legs elevated until all edema has disappeared. During this time, once the danger from embolus is safely past, the flow of blood should be promoted by massage, by warmth and, when the pain has subsided, by active movement. When the patient is ready to put his feet to the ground, the affected limb should be protected against venous distention by the application of a firmly fitted elastic stocking extending from ankle to knee and higher if it seems advisable. He should be instructed never to stand or

walk without this support. The patient should be warned against straining, lifting, constipation and pregnancy, and convalescence should be slow with respect to the length of time spent on the feet each day. After three months or thereabouts, when the heavyweight, single way stretch elastic stocking begins to get slack, he should be examined carefully for any of the signs of varicose veins or valvular incompetence and the circulation in his skin should be evaluated. If at this time it is evident that his leg is perfectly normal, he should be advised to wear a lightweight, two way stretch elastic stocking, which gives less support but is much more comfortable than the heavier one. At the end of one year and before the leg is allowed to go entirely without support, the patient should again be examined and made to walk around with the leg tightly bandaged as a method (Perthe's test) of testing the patency of his deep femoral veins. A record of this should be made. If at either of these examinations it seems that varicose or valvular incompetence is developing, the stronger support should be continued and the patient should be warned again of the possibility of permanent disability.

In such patients it is certainly less likely that deterioration of the skin, fibrosis and edema will develop if their incompetent veins are dealt with surgically. It is also possible that the early eradication of the incompetent saphenous system in such patients might contribute toward prevention of the development of the undesirable incompetences below the knee. It is even more probable that some of the valves below the knee actually are damaged in the first instance by the thrombotic process, though their incompetence, of course, does not show up until after the thrombus has resolved and the vessel recanalized. In spite of these indications for haste, it is obvious that no surgical work must be undertaken on the long saphenous system until the deep femoral system has demonstrably recanalized and is capable of carrying the whole venous return from an active limb. Moreover, it is felt that the presence of recent thrombophlebitis suggests the probability of a subacute dormant infection and that at least a year should be allowed to elapse after the first episode before it is safe to attempt surgical treatment on the veins of that leg. It should be added that, although one year is the usually advocated time, there seems to be a tendency to increase the time from one year to one and one-half years.

Although such a patient, if his saphenous system is demonstrably incompetent, can be expected to derive definite prophylactic value from surgical procedures, great care should be taken not to offer him anything which he may interpret as the prospect of a cure. After surgical treatment he should be followed carefully at six month intervals. Unusual care should be taken that any distended vein accessible from the surface, either by inspection or by palpation, is obliterated by sclerosing fluids, and every attempt should be made to observe the earliest signs of the onset of edema and to control it by every method available.

TREATMENT OF AN UNUSUAL SUBDURAL HYDROMA (EXTERNAL HYDROCEPHALUS)

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WHEN cerebrospinal fluid progressively accumulates over the surface of one or both cerebral hemispheres, the condition is known as external hydrocephalus, or subdural hydroma. It results from a tear in the arachnoid membrane, through which the fluid pours into the subdural space, where it cannot absorb. Moreover, when a peripheral branch of the subarachnoid space is involved the fluid is trapped in the subdural space as by a valve, the compression of the arachnoid by the fluid closing the opening and preventing its return into the subarachnoid space, although the fluid can and does continue to pass into the subdural space. It is now known that cerebrospinal fluid can be absorbed only in the subarachnoid space and from the capillaries of the pia-arachnoid. It cannot be absorbed in the subdural space (except in minimal amount). The end result of this sequence of events is a large quantity of fluid over one or both cerebral hemispheres, and the cerebral hemisphere or hemispheres are pushed downward toward the base of the brain.

There are two types of external hydrocephalus: 1. Congenital type. It is a sequel of internal hydrocephalus of the communicating type. Either from a congenital defect in the wall of the cisterna chiasmatis or from continued pressure of fluid in this cisterna the membrane ruptures and fluid pours over both cerebral hemispheres. The results are a tremendous bed of fluid in a greatly enlarged head and two tiny cerebral hemispheres crowded to the base of the skull. Valve action is absent in this type. An excellent example of this type of external hydrocephalus is produced at operation by an opening in the anterior part of the floor of the third ventricle for internal hydrocephalus. The fluid passes into the subdural instead of the subarachnoid space, and the internal hydrocephalus is then transformed into external hydrocephalus. I have since learned that by making the opening farther back in the floor of the third ventricle the fluid can be diverted into the subarachnoid space and this complication will be avoided. 2. A post-traumatic type. In this type the arachnoid membrane is torn beyond the cisterna; fluid then pours into the subdural space. This type is usually unilateral, since a peripheral branch of the arachnoid is involved and the fluid accumulates over one hemisphere only. Doubtless, many of the patients in such cases are

† Dr. Dandy died April 19, 1946.

cured spontaneously when the arachnoid tear heals. Others require evacuation and drainage of the fluid for a short time until the arachnoidal wound closes. The valve action in the causation of subdural hydroma should be stressed because of its importance. An opening in a cisterna will not induce a subdural hydroma, because the fluid is in free communication with the cisterna and will not therefore accumulate under pressure. The cisterna chiasmatis is routinely opened in many intracranial operations and never causes subsequent trouble.

The case presented here is one of the latter type but of unusual severity, i. e., despite repeated taps and drainage the accumulation of fluid continued, and without improvement. The entire hemisphere was depressed 5 or 6 cm. (fig. 4 *b*) from the dura, and a single vein (the rolandic vein) crossing from the hemisphere to the longitudinal sinus was stretched over the space. This type of case is doubtless rare; it is the only one I have seen resulting from trauma and assuming such magnitude and the only one that has not been amenable to repeated taps or temporary drainage, nor do I know of any other cases in the literature.

REPORT OF A CASE

D. H., an ill-looking, sparely nourished, very drowsy boy aged 2¼ years (fig. 1), entered the Johns Hopkins Hospital Aug. 24, 1944. He complained of severe generalized headaches. He had been well until April 1944 (four months previous), when he fell down a flight of steps. He was not unconscious, but the next day he was dizzy and vomited once. He was irritable for some time and was given phenobarbital. Two months later he fell off a table and immediately vomited and continued to vomit throughout the day. His physician found bilateral papilledema and increased reflexes on the right side. (The papilledema could not have developed so quickly and must therefore have been the sequel of the fall two months earlier). He was taken to Dr. Joseph P. Evans, of Cincinnati, who suspected a subdural hydroma; he tapped the subdural space in the occipital region of the left side, found a large amount of subdural fluid and drained it. When this was unsuccessful, he performed a left subtemporal decompression and again drained the fluid. Next, a left craniotomy was done over the decompression, which was tight and full. The fluid was evacuated, but it subsequently continued to collect under pressure.

The neurologic examination showed only a full and tight subtemporal decompression, a floating bone flap, hyperactive reflexes on the right, a positive Babinski sign on the right and a slight palsy of the left sixth nerve. There was no papilledema.

Operation.—On Sept. 13, 1944, air was injected into the spinal column; 300 cc. of fluid was removed and this amount of air injected. The ventricular system filled and was reduced in size and pushed to the right (figs. 2 and 3). A great bed of air covered the left hemisphere, which was also separated from the falx (figs. 2 and 3).

On September 15, the old craniotomy wound was reopened. The bone flap was lying loose and nowhere attached to bone. A tremendous amount of fluid covered the entire left hemisphere and depressed it fairly uniformly 5 or 6 cm.

below the dura (fig. 4); the hemisphere was separated from the falx. A thin avascular membrane lined the inner surface of the dura. Only one vein, the rolandic, crossed from the hemisphere to the longitudinal sinus. It was intact, but it was attenuated from its long stretch. The entire outer surface of the hemisphere could be inspected, and no sign of a tear in the meninges could be seen nor could any fluid be seen passing from the sylvian fissure or anywhere on the surface of the brain. The cisterna at the chiasm was normal but tore during the retraction. By elimination, it was suspected that the rupture of the arachnoid was along the falx, and this could not be inspected satisfactorily. The arachnoid along the falx had been suspected before operation because on

Fig. 1.—Photograph of patient before the operation, showing bulging decompression due to the pressure of the subdural hydroma. Note the slight palsy of the left sixth nerve.

a few occasions after tumors had been removed from the falx the fluid continued to pour out for a rather long period, and on two or three occasions it had been necessary to iodinize this membrane to hasten closure of the fistula. However, in this case there was no way by which the location of the probable fistula in the arachnoid could be determined. With a cotton pledget immersed in 3.5 per cent iodine, the surface of the hemisphere adjacent to the falx was swabbed from the frontal to the occipital pole (fig. 4 *A*). After about a minute, the iodinized area was washed with isotonic solution of three chlorides. The opening in the

cisterna chiasmatis (opened at operation) was also swabbed with iodine, the optic nerve being protected with a piece of cotton.

Subsequent Course.—The decompression remained full and tight until the thirteenth day, when it appeared smaller and softer, and during the succeeding ten days it steadily receded. On the twenty-fifth day the decompression suddenly became full and tight; the fluid contained 500 cells, with 80 per cent polymorphonuclears; the temperature rose to 103.8; the pulse rate was 144 and the white blood cell count 24,360. It was thought that the fluid had become infected from the subdural taps that had been made from time to time, but no organisms grew from the subdural fluid; the patient had just recovered from a severe cold. He was given sulfadiazine therapy, and he quickly improved. The decompression again became soft. Five weeks after operation the decompression was flat, and the patient was active and happy. He was discharged Oct. 31, 1944.

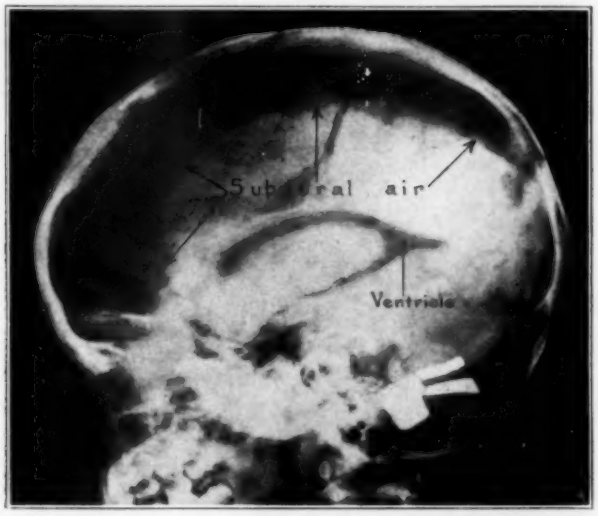

Fig. 2.—Lateral view (retouched) of encephalogram showing the tremendous accumulation of fluid (air) in the subdural space and the uniformly compressed lateral ventricle.

Subsequent Note.—On March 25, 1945, Dr. Evans stated, "I think that one must conclude that the boy is a normal child, but I still want to speculate as to whether you or Nature should be given credit for the result."

Since there is a tendency for spontaneous healing of subdural hydromas, Dr. Evans' query is quite natural. However, this patient had gone four months, and neither repeated taps nor drainage had been at all helpful. Moreover, the closure of the fistula had occurred promptly, i. e., thirteen days after operation, when the decompression became soft. This is about the time one would expect a fistula to close from adhesions induced by iodine. It is true that a definite fistula was not disclosed because it was in a part of the subarachnoid space that

could not be inspected. Whether or not it could have been actually seen if inspection were possible is doubtful. However, it appeared that this was the logical place to expect the leak, since the meninges elsewhere were intact and because from past experiences it had been learned that openings in the subarachnoid space along the falx were more refractile to spontaneous closure than elsewhere. Since the fistula could not be seen, it was necessary to iodinize the entire area along the falx to insure its inclusion.

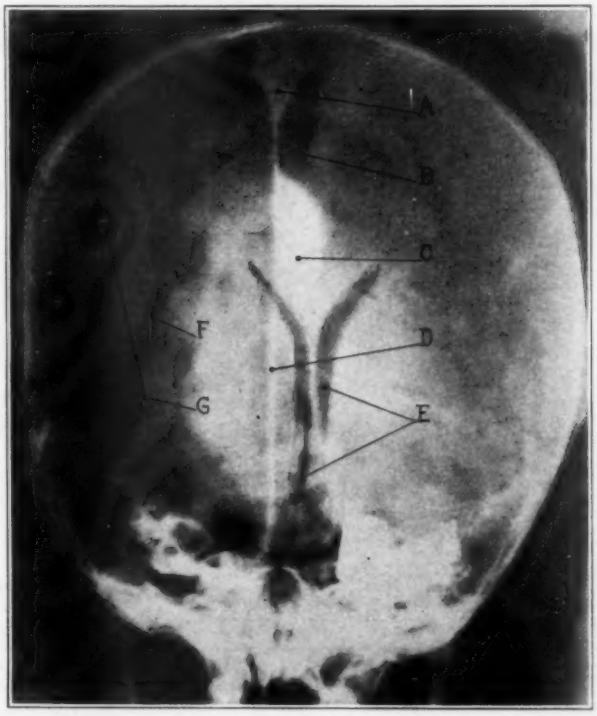

Fig. 3.—Anteroposterior view (slightly retouched). This shows: *A*, the triangular falx at the longitudinal sinus; *D*, the falx elsewhere (these shadows are set off by the air in the subdural space); *B*, a small amount of air along the falx on the right (opposite) side; *C*, unexplained shadow, doubtless also set off by the air in the subdural space (this cannot be seen in the lateral view); *E*, lateral and third ventricles pushed to the right side; *F*, defect in bone, created when flap was made, and *G*, subdural air on the left side.

INTERPRETATION OF ENCEPHALOGRAMS

There are some details in the air plates—particularly in the anteroposterior views—that are difficult to interpret; they may or may not be significant. It has been stated that in this case the external hydrocephalus (hydroma) was unilateral. Subdural taps on the right side encountered no fluid, and there was no fluid over the right cerebral

hemisphere. However, in the anteroposterior view there appears to be a small pocket of air between the falx and the hemisphere on the right side (fig. 3 *B*); with stereoscopic vision, this can be located well anteriorly and appears to be an isolated pocket. It is possible that this shadow may not be on the right side but may be part of the left air shadow pushed over to the right side. However, to the left of this air shadow is a triangular opaque shadow of the falx (fig. 3 *A*) at the longitudinal sinus. It is outlined because air is on both sides; moreover, it is in the exact midline of the skull.

There are two other features that have been consistently present in repeated plates, and the explanation for them is not too clear. 1. There

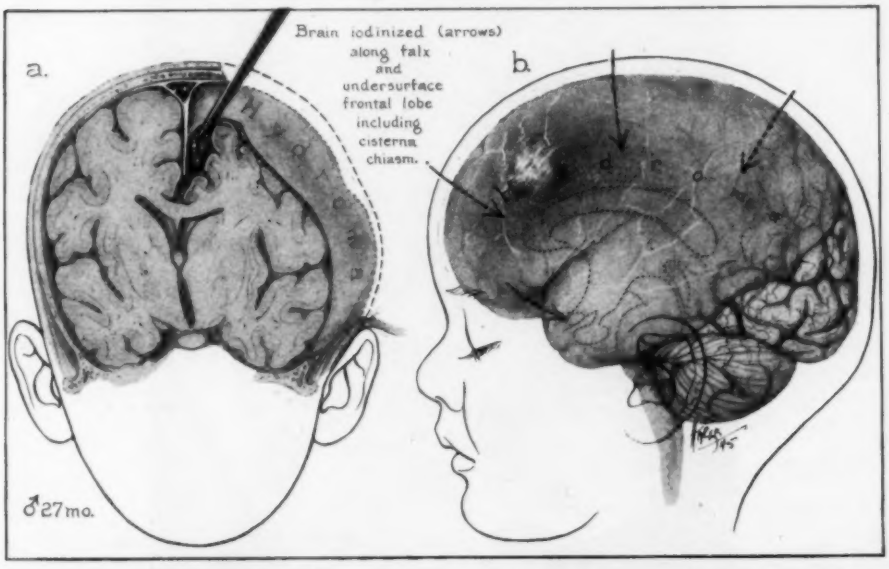

Fig. 4.—Drawing showing (*b*) the subdural collection of fluid and (*a*) the method of swabbing the mesial surface of the hemisphere with iodine to promote adhesions and closure of the fistula.

is a sharply outlined line through the center of the head (anteroposterior view), with a slight bulge to the right (fig. 3 *D*). This is almost certainly the falx and is continuous with the triangular shadow of the falx noted above. But, unless there is air on both sides of the falx, there is no reason that the falx should be so sharply delineated. The probable explanation is that there is air on both sides of the falx, but it cannot be seen in the roentgenogram. A shadow of this kind I have not seen before.

2. The most difficult shadow to interpret is an oblong opacity in the anteroposterior view (fig. 3 *C*); it is about 1.5 cm. long and 1 cm. wide and is attached to the midline linear shadow and is on the right side.

With stereoscopic vision this can be seen well anteriorly in the frontal region. Repeated attempts have failed to locate this shadow in the lateral view. It, therefore, is not a calcification but must be a soft tissue shadow, thrown in relief by the surrounding air, which is not visible. The significance of this opaque shadow is not clear, but the question arises whether it may be a congenital lesion, perhaps a precursor of a subsequent calcification of the falx, and possibly indicates the point at which the rupture of the meninges has occurred. My guess would be that this may be true, but proof is lacking. Subsequent cases may throw additional light on these findings.

It will be noted in the lateral view that the left lateral ventricle is small and depressed (fig. 2) by the downward displacement of the hemisphere. There is a pronounced shift of the ventricular system to the right (fig. 3 *E* [anteroposterior view]).

RELATION OF SUBDURAL HYDROMA TO ABSORPTION OF CEREBROSPINAL FLUID

This case is also of interest because of its bearing on the place and manner of absorption of cerebrospinal fluid. There are two schools of thought on this point: (1) that the fluid is absorbed from the entire subarachnoid space and into the capillaries of the pia-arachnoid (this is my own view and is based on experiments that have been described); (2) that the fluid passes into the longitudinal sinus by way of the pacchionian granulations or other preformed stomas in the walls of the longitudinal sinus (this is the conception of Weed).

If one views the condition superficially, the tremendous bed of fluid over the cerebral hemisphere in this patient might appear to be an ideal example of the effects of closure of openings through the pacchionian granulations or their equivalents, i. e., postulated microscopic stomas in the longitudinal sinus. However, this conclusion is not so simple as it seems, for the fluid is in the subdural space and not in the subarachnoid space. If such postulated openings were obstructed, the fluid must be in the subarachnoid space and must cover the hemisphere, for it must dam back from the point of obstruction. Not only is that not true in this case, but it might be added that in well over a hundred of my cases that have come to operation and necropsy such a condition has never yet been observed.

Moreover, if this bed of fluid in the subdural space were due to blockage of such hypothetic openings, there could be no possibility of curing the condition. Certainly the openings could not be reestablished and regain function after being closed for four months. On the other hand, the separation of the hemispheres from the longitudinal sinus in this case is precisely like that in the experiments on dogs, in which the hemispheres are separated from the longitudinal and transverse sinuses

on both sides (there is only one attachment, i. e., the rolandic vein, and there are no pacchionian granulations) and without the slightest effect on the absorption of cerebrospinal fluid; nor does fluid accumulate over the cerebral hemispheres thereafter.

The deduction is clear that the postulated openings in the longitudinal sinus have no foundation; in fact, they do not exist. The absurdity of openings into veins is shown by the fact that blood would pass out of them into the subarachnoid space as easily as fluid could pass into them. Veins just do not have openings in their walls. Cerebrospinal fluid is absorbed from the capillaries of the pia-arachnoid, and its absorption is precisely similar to that of fluids elsewhere in the body.

DIAGNOSIS OF ACUTE APPENDICITIS IN THE PRESENCE OF DIARRHEA

E. L. KEYES, M.D.
AND
M. M. COOK, M.D.
ST. LOUIS

IN THE presence of diarrhea the differential diagnosis of acute appendicitis from enteritis is difficult. Even in the absence of diarrhea acute appendicitis may be mistaken for enteritis because both diseases begin with pain not unlike a sensation of impending diarrhea and because the physical and the laboratory findings may be almost identical in the two diseases during the early stage (cases 2 and 3).

TABLE 1.—*Differential Diagnosis of Early Acute Appendicitis and Enteritis*

Point	History	Acute Appendicitis, Early Stage	Enteritis
1	Pain	Persistent in midline despite defecation	Varying situation; intermittent; relieved by defecation completely if temporarily
2	Bowel urge	Associated with pain; persists despite defecation	Associated with pain; relieved by defecation completely if temporarily
3	Diarrhea	Uncommon; subordinate to bowel urge	May dominate clinical picture
4	Nausea	Subordinate to bowel urge; occurs subsequent to pain	May exceed bowel urge; may precede pain
5	Vomiting	Present in less than half the cases	Present in over half the cases
		Physical Findings	
6	Tenderness	None in some cases; epigastric, perumbilical or rectal in others	None in some cases, variable in others; bowel sounds may be hyperactive
		Laboratory Findings	
7	Fever	None or slight	Same
8	White blood cell count	Usually over 10,000	Lower average

Points 1 to 4 under acute appendicitis constitute the "gas stoppage sensation."

Ultimately, the diagnosis may depend largely on the results of an orderly and detailed analysis of the history of the case, which brings out points 1 to 4 listed in table 1. The differential points are as follows: The first pain of acute appendicitis is persistent, and that of enteritis is intermittent. The first pain in both ailments is associated with a bowel

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urge,[1] but pain persists despite defecation in the early stage of acute appendicitis whereas in enteritis defecation relieves the pain completely if temporarily. Moreover, in early acute appendicitis the downward urge to defecate exceeds the upward urge to vomit whereas the converse often occurs in enteritis. Finally, diarrhea when present often dominates the clinical picture in enteritis, whereas early in acute appendicitis it is the bowel urge, not the diarrhea, which chiefly occupies the attention of patients. Such are the points we wish to make in this paper.

REPORT OF ILLUSTRATIVE CASES

Failure to appreciate points 1 to 4 (table 1) caused dangerous delay in diagnosis, for diarrhea clouded the clinical picture of acute appendicitis.

A consultant not familiar with points 1 to 4 in table 1 saw the patient in the following case during the second day of illness, on Monday evening (chart 1, C_1), with a clinical picture as given in the following report.

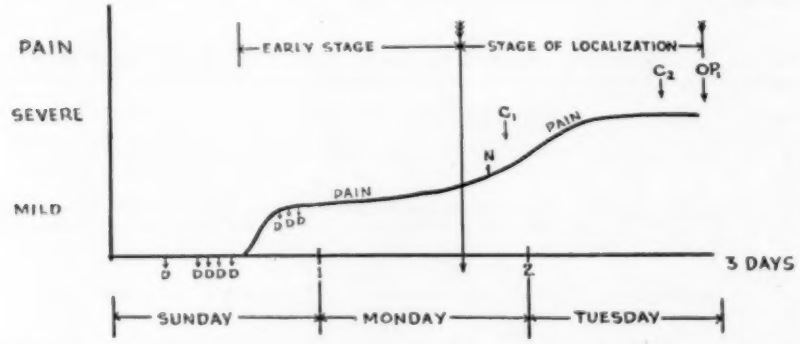

Fig. 1 (case 1).—Pain chart in acute appendicitis. *D* indicates diarrhea; *N*, nausea; C_1, first consultation; C_2, second consultation, and *Op*, operation. Note that pain persists despite diarrhea.

CASE 1.—W. S. B., a 41 year old man, was admitted to the hospital Nov. 14, 1944.

Previous History.—The patient had had diarrhea for a day one week previous. His wife had also had diarrhea then.

Present Illness.—Diarrhea recurred the day before consultation. It was painless at first, but that afternoon it was associated with what the patient called "a little knot or tight feeling just below the belly button." The patient ate a heavy supper Sunday night and then lay down because, he said, "the tight feeling persisted." After supper, he went to the toilet three times and "had a loose movement each time, with no relief." He took camphorated tincture of opium and magnesium hydroxide. Monday afternoon, before the time of his first consultation, the pain began to shift to the right lower quadrant of the abdomen and the patient felt nauseated.

1. Keyes, E. L.: Diagnostic Features of the First Pain of Acute Appendicitis, J. Missouri M. A. **41**:30-33 (Feb.) 1944.

Physical Findings.—There were tenderness and muscle guard in the right lower quadrant of the abdomen.

Laboratory Findings.—The white blood cell count was 14,000.

Comment.—It was the history of the presence of diarrhea that alone raised doubt in the mind of the first consultant as to the validity of the diagnosis of acute appendicitis on Monday evening (chart 1, C_1). Otherwise the clinical picture was typical of acute appendicitis. The presence of diarrhea, however, suggested enteritis as a possible diagnosis, a supposition that was strengthened by the fact that both the patient and his wife had had enteritis the week before. These doubts caused a day's delay in diagnosis, for the significance of the points in table 1 was not fully appreciated by the first consultant.

By the next day all doubts as to diagnosis were dispelled (chart 1, C_2). Signs of localization had become unquestioned. A surgeon (E. L. K.) was called, and immediate operation was recommended. The appendix was found completely gangrenous and ruptured, and peritonitis was present. The appendix was removed. Recovery was slow.

TABLE 2.—*Criteria for the Diagnosis of Acute Appendicitis in the Early Stage*

History	Midline pain associated with bowel urge persisting for hours despite defecation and despite diarrhea; the downward urge to defecate exceeds the upward urge to vomit; this syndrome is named the "gas stoppage sensation"; pain precedes nausea; fewer than 50 per cent of patients vomit
Physical findings	Tenderness in the epigastrium, about the umbilicus or by the rectum; no tenderness whatsoever in some cases
Laboratory findings	Temperature normal or slightly elevated; pulse normal or slightly accelerated; white blood cell count over 10,000 indicates acute appendicitis histologically; white blood cell count under 10,000 indicates subacute or obstructive appendicitis or lesser changes histologically [2]

Undelayed diagnosis was made in the early stage of a comparable case of acute appendicitis, despite the possibility of impending diarrhea, by use of the criteria in tables 1 and 2.

The patient in the following case (case 2) was first seen (chart, 2, C_1) by one of us (E. L. K.) at a time comparable to the time of first consultation in the previous case, namely, the second day of illness, and with a comparable history with respect to the passage of many stools. Despite the fact that this patient had had five stools, enteritis or impending diarrhea were not thought the likely diagnosis, but instead a diagnosis of acute appendicitis was made, although signs of localization as yet had not appeared. Definitive and undelayed diagnosis proved possible by use of the criteria in tables 1 and 2.

Particular emphasis in the diagnosis in case 2 was placed on the history of prolonged persistence of the midline pain, pain which persisted over twenty-four hours, pain which was associated with the urge to defecate and pain which persisted despite the five bowel movements. Pain, moreover, was midline in situation. Note, before the findings in the case are divulged, that the criteria in tables 1 and 2 are fulfilled by the clinical picture, which may now be presented.

CASE 2.—B. B., a 22 year old man, was admitted to the hospital June 24, 1944.

Previous History.—On Thursday, the patient was constipated and took a laxative. There was no pain then.

Present Illness.—On Friday, mild "generalized cramps" began. They persisted during Saturday, and the patient on that day passed five solid stools. Before supper Saturday night, he said, he "didn't feel so good" so he "sat on the toilet," thinking that if he "could pass gas it would relieve" him but, although gas was passed, pain persisted and after the patient had eaten a good supper, he said, "it kept bothering me more and more," becoming "just a continual gripe" about the umbilicus and the epigastrium. Just before the first consultation, he felt nauseated.

Physical Findings.—There was slight tenderness in the epigastrium and in the rectum but none elsewhere.

Laboratory Findings.—The patient's temperature was 101.2 F. and the white blood cell count 10,100.

Comment.—Immediate operation was recommended (E. L. K.) on the basis of these criteria (table 2), but the patient requested a second opinion, which could

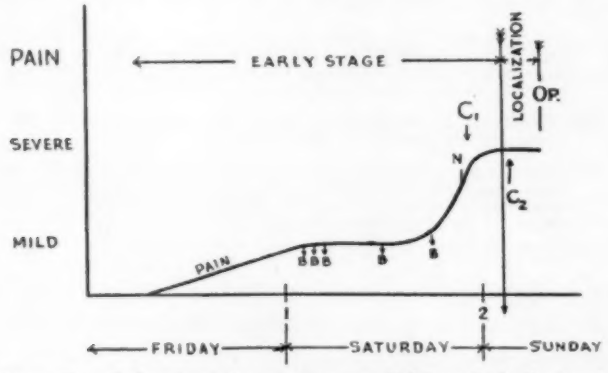

Fig. 2 (case 2).—Pain chart in acute appendicitis. *B* indicates bowel movement; *N*, nausea; C_1, first consultation; C_2, second consultation, and *Op*, operation. Note that pain persists despite defecation.

not be obtained for some hours; operation nevertheless was scheduled. During the intervening hours, the pain shifted to the right lower quadrant of the abdomen and signs of localization appeared. At operation the appendix was found greatly distended by increased pressure within the lumen, resulting from its complete blockage by a large fecalith impacted in the base. Following appendectomy, recovery was rapid. The histologic diagnosis was acute appendicitis.[2]

CRITERIA FOR THE DIAGNOSIS OF ACUTE APPENDICITIS IN THE EARLY STAGE (TABLE 2)

The criteria in table 2 often warrant the early diagnosis of acute appendicitis prior to the time of localization, in our experience. These criteria are not widely taught. Ordinarily, it is taught that diagnosis

2. Histologic diagnoses in the cases reported in this paper made by Dr. N. A. Womack and Dr. Charles Eckert of the Department of Surgical Pathology.

should be delayed until the criteria for the later "stage of localization" become manifest.

Appendicitis passes through a state of pathologic development which may roughly be divided into two stages—an early stage and a later stage of localization. In the early stage inflammatory changes remain confined to the appendix; Wilkie [3] and Wangensteen [4] have shown experimentally how inflammation and infection can arise from obstruction of the lumen of the appendix. In the later stage of localization, inflammation spreads from the appendix to the mesoappendix and the parietal peritoneum.

The early stage corresponds generally to the "early afebrile stage" of Wilkie [3] and to the stage in which Eusterman [5] said "a vague

TABLE 3.—*Time Element in Differentiating Enteritis from Early Stage of Acute Appendicitis*

A. Time Elements of the Pain of Enteritis *

	Case 5	Case F. D.	Case 3	Case T. H. G.	Case 7	Average
Individual cycle of pain						
Duration of each pain.....	½ min.	3 to 4 min.	5 to 10 min.	20 min. or 10 sec.	....	....
Duration of pain-free intervals	5 min.	3 to 4 min.	20 to 30 min.	60 min. or 30 sec.	....	....
Total duration of attack.....	6 hr.	11 hr	12 hr.	10 hr.	7 hr.	9 hr.

B. Total Duration of Attack of Enteritis Compared with Duration of the Early Stage of Acute Appendicitis †

	Enteritis (5 Cases)	Acute Appendicitis, Early Stage (20 Cases)
Average duration.....	9 hr.	20 hr.
Shortest duration.....	6 hr.	1 hr.
Longest duration.....	12 hr.	3 days

* Cycles of pain are irregular. The average attack lasts nine hours.
† Pain persisted on the average of twenty hours in the early stage of acute appendicitis.

dyspepsia may precede for some time an acute localizing seizure." The early stage lasts twenty hours on the average (table 3). In some patients it lasts an hour or less. In others it may last two or three days (case 1).

Prolongation of the early stage may result in dangerous delay in diagnosis (case 1) or even in death (Devine [6]). Authors have criticized

3. Wilkie, D. P. D.: Acute Appendicitis and Acute Appendicular Obstruction, Edinburgh M. J. **25**:308 (Nov.) 1920.

4. Wangensteen, O. H., and Dennis, C.: Experimental Proof of the Obstructive Origin of Appendicitis in Man, Ann. Surg. **110**:629-647 (Oct.) 1939.

5. Eusterman, G. B.: Notes on the Dyspepsias, with Special Reference to Diagnosis, J. Missouri M. A. **9**:329-332, 1913.

6. Devine, H.: The Surgery of the Alimentary Tract, Baltimore, Williams & Wilkins Company, 1940.

the lack of accepted criteria for diagnosis in the early stage. Regarding current criteria for diagnosis, which are criteria for diagnosis in the later stage of localization, Zachary Cope [7] commented, "The so-called typical symptoms of appendicitis as given in textbooks often indicate a somewhat advanced stage of the condition." Delay in diagnosis until the third day is common and is also dangerous because the appendix ruptures on the third day on the average.[8]

To make the diagnosis of acute appendicitis in the early stage requires great reliance on the results of careful analysis of the history of the case, for the early physical findings are inconclusive (table 2). Eusterman says that in "appendiceal dyspepsia, pain is not referred to McBurney's point, and often no appendiceal tenderness can be elicited." Leukocytosis, however, is usual, the count often being over 10,000.

So characteristic do we believe the pain of acute appendicitis to be in the early stage that it has been given the name of the "gas stoppage sensation." The reason for this inadequate name is that a patient is apt to feel that if he "could pass gas" he might obtain relief from the "continual gripe" (patient 2) or "tight feeling" (patient 1) or whatever name the patient may give the first pain.

The "gas stoppage sensation" comprises persistent midline pain associated with a bowel urge, which causes patients to seek the toilet and to take laxatives.[9] Pain persists for hours or for days. Pain persists despite defecation, despite diarrhea and despite the passage of gas by rectum. The downward urge to defecate exceeds the upward urge to vomit. So mild may be the sensation as to be overlooked by some patients. It is severe in other patients, often made worse by eating, by exertion and by catharsis. The "gas stoppage sensation" disappears usually as localization begins. It is a subjective sensation. It is a symptom. It is not a physical sign.

The "gas stoppage sensation" is claimed to be characteristic of the early stage of acute appendicitis for the following reasons. Three surgeons (E.L.K. included) and one internist have personally felt the sensation prior to the removal of their own acutely inflamed or gangrenous appendixes. Dr. P. O. Thomas and one of us (E.L.K.) recently elicited a history of the "gas stoppage sensation" at onset in 58 of 76 successive patients with acute appendicitis histologically proved at the St. Louis City Hospital and in private practice. We

7. Cope, Z.: The Early Diagnosis of the Acute Abdomen, ed. 8, London, Oxford University Press, 1940.

8. Keyes, E. L.: Death from Appendicitis: The Mortality from Appendicitis and the Causes of Death Following Appendicitis, Ann. Surg. **99**:47-68 (Jan.) 1934.

9. Keyes, E. L., Jr.: The Sensation of Gas Stoppage During the Onset of Acute Appendicitis, with Illustrative Cases, Surgery **17**:270-283 (Feb.) 1945.

found it absent chiefly in children under 7, too young to comprehend the three questions used to elicit it, and otherwise in patients with low intelligence quotients, as pointed out by Dr. Mitchell Johnson. Dr. John Akin found it present at onset in most of the cases of acute appendicitis at Barnes Hospital. From these calculations one may expect to find histories typical in this respect in about 3 or 4 patients out of every 5.

Almost as striking as the presence of the sensation at onset of acute appendicitis is its consistent absence in acute conditions within the abdomen of other types, with the exceptions hereafter noted. The "gas stoppage sensation" has been found absent in every patient with perforated peptic ulcer, renal disease, gallstone colic and acute cholecystitis with but one exception, in a woman with acute cholecystitis. The sensation has been found absent in many cases of acute salpingitis at the St. Louis City Hospital by Dr. Lyle Bachman, though one of us (E.L.K.) has noted two exceptions to this rule. The sensation

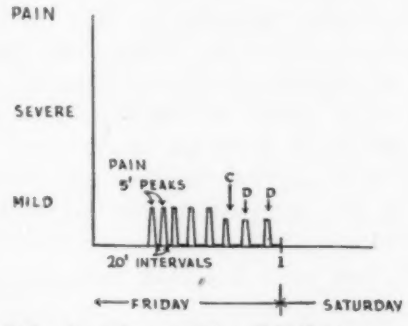

Fig. 3 (case 3).—Pain chart in enteritis. *C* indicates consultation and *D*, diarrhea. Note that pain is relieved temporarily by defecation.

has been found absent in all but 2 cases of ruptured ectopic gestation (E.L.K.). It has been found absent in 150 cases of enteritis (M.M.C.), as we are in the process of discussing. However, in one surgical condition it does occur consistently at onset (E.L.K.), namely, at onset of acute intestinal obstruction of the small bowel, although in such cases vomiting rapidly comes to exceed the downward urge.

Pain in enteritis is intermittent (table 1 point 1).

Case 3.—J. W. G., a man aged 22, was admitted to the hospital Feb. 16, 1945.

History.—The patient said that in the morning, about 9 o'clock, he noticed "intermittent pains, which would hurt five or ten minutes and then disappear for a while." Disappearance of pain was complete between pains. The pain was situated just below the umbilicus. Bowel urge accompanied the pains, and there was anorexia.

Physical Findings.—There was tenderness about the umbilicus but no tenderness by rectum.

Laboratory Findings.—The patient's temperature was 98.6, and the white blood cell count was 13,300, with shift.

Comment.—At the time of the first consultation (chart 3 *C*), because pain was associated with the bowel urge and because there was tenderness about the umbilicus and leukocytes with shift, a diagnosis of acute appendicitis in the early stage was considered by us. However, the pain was intermittent. Pain lasted only five or ten minutes; then there was complete relief. Moreover, the attack was but six hours old. Consequently, the diagnosis of enteritis was made. The diagnosis proved correct when later that night the patient passed two diarrheal stools (chart 3, *DD*). By the next morning he was completely well.

One year later, on Feb. 25, 1946, he was operated on for acute appendicitis (E.L.K.). The pain of his attack of acute appendicitis differed from the pain of his attack of enteritis, he said, with respect to the points discussed in this paper.

Compare the clinical picture in cases 2 and 3, and note that the main difference is with respect to the pain. The pain in this case of enteritis (case 3) was intermittent. The pain in the patient with appendicitis (case 2), by comparison, was persistent. He said that it was "just a continual gripe," lasting over twenty-four hours.

The difference between "intermittent" and "persistent" as used in this paper is a difference in periods. Table 3 indicates this point. The intermittent pain of enteritis lasts a matter of minutes and then disappears again for a matter of minutes. The persistent pain of beginning acute appendicitis lasts for many hours or even for some days. Only in recurrent appendicitis does pain remit completely and then recur. This is not intermittent pain but rather, as Eusterman called it, "a continuous pain" which occurs in "distinct prolonged attacks." To clarify this point it will be necessary to present another case (case 4).

Pain in recurrent appendicitis occurs in distinct prolonged attacks.[5]

CASE 4.—B. F. S., a 24 year old man, was admitted to the hospital June 9, 1945.

History.—Wednesday, after eating dinner, this patient said that he noticed a "full feeling in the stomach" and then a "dull aching in the epigastrium." Next, he said, he passed a diarrheal stool, "with no relief from pain." Later he was nauseated. The first attack lasted eighteen hours, from Wednesday to Thursday; then it subsided, and the patient felt no pain whatever. Three further distinct attacks occurred, lasting four, eleven and eighteen hours respectively. Between attacks, pain disappeared.

Physical Findings.—There was tenderness in the epigastrium but none elsewhere. The rectal examination revealed no abnormalities.

Laboratory Findings.—The temperature was 99.2 F., and the white blood cell count was 11,600, without shift.

Comment.—A diagnosis of recurrent appendicitis was made by us at the time of first consultation, Saturday afternoon (chart 4 *C*), by use of the criteria in table 2. Immediate operation was recommended, but pressing schoolwork required its postponement. Meanwhile, the patient being under close observation in the hospital, the attack subsided. The next week operation was performed; the

appendix still seemed boggy; it contained a fecalith and was removed. Histologically, the diagnosis was chronic obstructive appendicitis, and there was evidence of recent inflammation.[2]

Pain in enteritis is relieved by defecation completely if temporarily.

CASE 5.—T. E., a 23 year old man, was admitted to the hospital in June 1944.

History.—This patient noted "cramps in the lower part of the abdomen which would last thirty seconds and which occurred periodically at intervals of about five minutes." He said, "I had no symptoms between cramps. After about forty-five

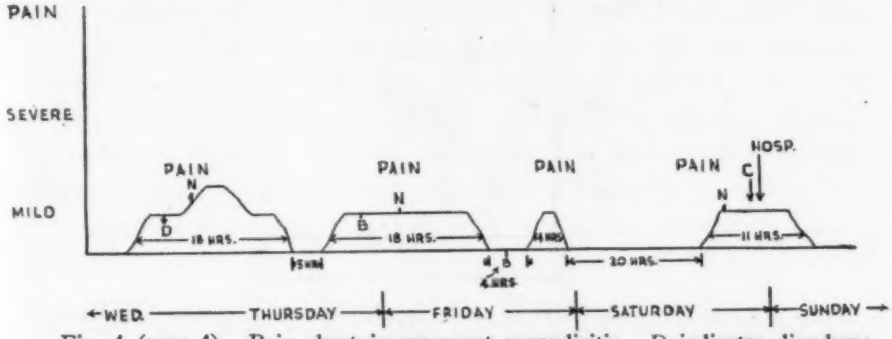

Fig. 4 (case 4).—Pain chart in recurrent appendicitis. *D* indicates diarrhea; *N*, nausea; *B*, bowel movement; *C*, consultation, and *Hosp.*, hospitalization. Note how many hours pain persists.

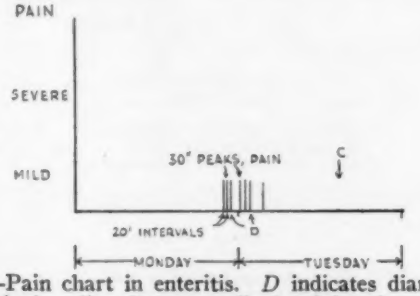

Fig. 5 (case 5).—Pain chart in enteritis. *D* indicates diarrhea and *C*, consultation. Note that pain is relieved temporarily by defecation.

minutes, I defecated. After moving my bowels, I felt completely relieved of symptoms." The cycle of pain was then repeated, and he said, "Funny thing, after I defecated I felt fine."

Physical Observations.—There were no abnormal findings.

Laboratory Observations.—The condition of the patient was normal.

Comment.—A diagnosis of enteritis was made. Operation was not performed. The first consultation was twenty-four hours after onset. Note that "after moving the bowels, I felt completely relieved of symptoms," said the patient.

Pain in the early stage of acute appendicitis persists despite defecation and despite diarrhea (table 1, point 2).

CASE 6.—H. W., a 24 year old man, came to the hospital Jan. 23, 1945.

History.—This patient said, "At 11 a. m. today I noticed cramplike pain in the epigastrium." After eating lunch "I tried to have a bowel movement, and it

was extremely small; cramps became increasingly worse." Numerous stools made him think that "I was going to have diarrhea," yet pain persisted and he "still felt like I had to go to the toilet." He vomited once, but the downward urge predominated. The pain shifted to the right lower quadrant of the abdomen.

Physical Findings.—There was tenderness, muscle guard and rebound at McBurney's point. There was also rectal tenderness.

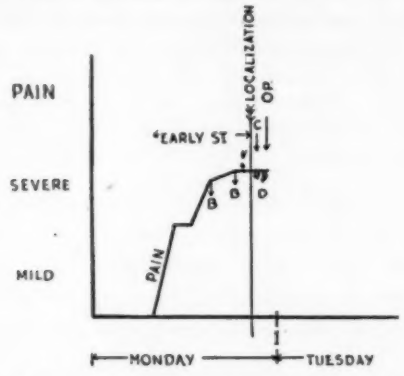

Fig. 6 (case 6).—Pain chart in acute appendicitis. *B* indicates bowel movement; *V*, vomiting; *C*, consultation, and *Op*, operation.

TABLE 4.—*Differential Diagnosis of Acute Appendcitis in the Stage of Localization from Enteritis*

Point	History	Acute Appendicitis, Late Stage	Enteritis
1	Pain	Shifts to right lower quadrant of the abdomen; may shift elsewhere; may fail to localize	Rarely shifts
2	Bowel urge	Usually disappears	Usually persists intermittently
		Physical Findings	
3	Tenderness	In right lower quadrant of the abdomen, increasing toward McBurney's point; may be atypically situated; occasionally absent; rectal tenderness common	Usually less pronounced and more variable in situation; bowel sounds may be hyperactive
4	Spasm and rebounds	Common; cough and rebound tenderness common [12]	Rare
		Laboratory Findings	
5	Fever	Normal to 102, occasionally higher	Lower or higher
6	White blood cell count	Average 15,100 to 15,900 (Ochsner, A., and Johnston, G. H.: Surgery **17**: 873, 1945)	Average 12,400 [21]

Laboratory Findings.—The patient's temperature was 98 and the white blood cell count 23,800, with shift.

Comment.—A diagnosis of acute appendicitis was made within twelve hours of onset, by criteria in tables 2 and 4. Appendectomy was performed immediately. The appendix was grossly and histologically inflamed acutely. The patient made a rapid recovery.

Persistence is a well recognized attribute of pain in the early stage of acute appendicitis; Homans,[10] for instance, wrote that "pain . . . early . . . partakes of the nature of a colic—a sustained colic, not an intermittent one."

Persistence of pain despite defecation is not well recognized as an attribute of the pain in the early stage of acute appendicitis. Yet this point is helpful in diagnosis. Persistence of pain despite defecation, despite diarrhea and despite the passing of gas by rectum is one of the most characteristic features of the pain of onset of acute appendicitis.

The patient in case 6 said that he thought that he "was going to have diarrhea." Then he defecated; yet pain persisted despite defecation. Knowledge of this fact aided us in making the diagnosis of acute appendicitis, although diagnosis was otherwise not hard here because pain had localized by the time of the first consultation.

Diarrhea in enteritis may overshadow the pain and the bowel urge (table 1, point 3).

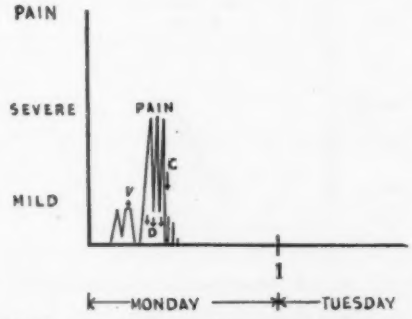

Fig. 7 (case 7).—Pain chart in enteritis. *V* indicates vomiting; *D*, diarrhea, and *C*, consultation.

Case 7.—W. A., a youth aged 20, was admitted to the hospital Dec. 11, 1944.

History.—The patient said that he awoke suddenly at 4:30 that morning, with a generalized "cramping sensation" accompanied with bowel urge, partially relieved by passing gas. He dozed and then awoke at 7 o'clock and vomited, with "relief for a minute." Then he "had a bowel movement. The first one was normal. That was just like uncorking things, and I spent the next hour on and off the toilet," passing watery stools, each of which "was preceded by considerable pain; in between, I curled up on the davenport and moaned to the boys in the other room (of the fraternity house), and they moaned back to me." His friends had been similarly affected, apparently from eating pumpkin pie with whipped cream at noon and in the evening of the previous day. By the time of the first consultation, seven hours after onset, he said that he "felt all right, except once in a while I get a little cramping."

10. Homans, J.: Textbook of Surgery, ed. 5, Springfield, Ill., Charles C Thomas, Publisher, 1940.

Physical Findings.—The patient had a McBurney scar from a previous appendectomy. There was tenderness throughout the abdomen, especially in both lower quadrants of the abdomen. The bowel sounds were hyperactive.

Laboratory Findings.—The temperature was 98.4 F. and the white blood cell count 17,600, with shift.

Comment.—A diagnosis of enteritis due to food poisoning was made. The patient made a prompt recovery. Note how diarrhea dominated the clinical picture.

Diarrhea if present in the early stage of acute appendicitis is subordinate to the painful bowel urge (table 2, point 3).

CASE 8.—D. D. C., a 20 year old youth, came to the hospital Jan. 28, 1945.

History.—The patient said that he "awoke Sunday morning with the desire to go to the toilet." He passed two liquid stools, with no pain. He said, "That afternoon I again had a desire to go to the toilet, but this time there was quite a bit of pain around the navel; it felt similar to pain when one takes an enema. I had the desire to 'go,' but it felt like something blocking it." He passed another liquid stool and later tried defecation again but unsuccessfully. The pain persisted and was worse when the patient was coughing or walking.

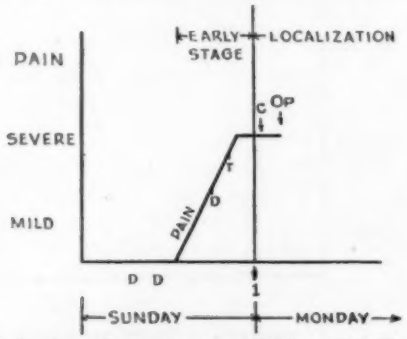

Fig. 8 (case 8).—Pain chart in acute appendicitis. *D* indicates diarrhea; *T*, trip to toilet; *C*, consultation, and *Op*, operation.

Physical Findings.—There was tenderness in the epigastrium and the right lower quadrant of the abdomen, increasing toward McBurney's point. There were muscle guard, rebound tenderness and tenderness by rectum.

Laboratory Findings.—The temperature was 99 F., and the white blood cell count was 19,550, with a shift.

Comment.—A diagnosis of acute appendicitis was made within twenty-four hours of onset, at first consultation, by criteria in tables 2 and 4. An acutely inflamed appendix was removed, and the diagnosis was confirmed histologically. Recovery was rapid.

Note that, despite diarrhea, pain and bowel urge dominated the clinical picture.

VOMITING

1. In Acute Appendicitis.—Vomiting probably occurs less often in acute appendicitis than some authors would lead one to suppose.[11]

11. Cole, W. H., and Elman, R.: Textbok of General Surgery, ed. 4, New York, D. Appleton-Century Company, Inc., 1944.

Our figures indicate that nowadays fewer than 50 per cent of patients vomit by the time they are operated on (table 5): The time of vomiting remains to be determined, whether it is relatively commoner during the early stage or during the stage of localization.

It seems important that in the early stage the urge to vomit is subordinate to the urge to defecate. The order of symptoms also is important. Pain always precedes nausea and vomiting in acute appendicitis.

2. In Enteritis.—Quigley and Contratto [12] estimated that about twice as many patients with enteritis vomit compared with the number of patients with acute appendicitis who vomit.

TABLE 5.—*Incidence of Vomiting in Acute Appendicitis*

Author	Number of Patients Vomited	Total Number of Patients
Spencer, J. H., Jr.: Am. J. Surg. **61**: 249, 1943	57	100
Quigley and Contratto [12]	23	60
Keyes, E. L.: Unpublished data from Barnes Hospital, 1944	10*	24
Totals	90	184

* Seven of these vomited in early stage.

Conclusion: Fewer than 50 per cent of patients with acute appendicitis vomit by the time they are seen nowadays.

MILDNESS OF ONSET OF SYMPTOMS

1. Acute Appendicitis.—Eusterman [5] wrote that "often a vague dyspepsia may precede for some time an acute localizing seizure" of appendicitis. Vague or mild onset of this sort was observed in patients 1, 2 and 4 of this series and in many others.

Both Reginald Fitz [13] and John B. Murphy [14] called the onset "sudden, severe," while Wilkie [15] called it "very acute and spasmodic at first." Severe onset of this sort was observed in the patient in case 6 of this series, while the initial mild pain of the patient in case 2 became severe just prior to the stage of localization.

12. Quigley, T. B., and Contratto, A. W.: The Differential Diagnosis of Acute Appendicitis and Acute Gastroenteritis in College Men, New England J. Med. **226**: 787-790 (May 14) 1942.

13. Fitz, R. H.: Perforating Inflammation of the Vermiform Appendix, with Special Reference to Its Early Diagnosis and Treatment, Tr. A. Am. Physicians **1**:107-144, 1886.

14. Murphy, J. B.: Surgery of the Appendix Vermiformis, in Keen, W. W.: Surgery: Its Principles and Practices, Philadelphia, W. B. Saunders Company, 1908, vol. 4, pp. 727-796.

15. Wilkie, D. P. D.: The Etiology of Acute Appendicular Disease, Canad. M. A. J. **22**:314-316 (March) 1930.

More careful study of the early stage will oftener reveal a mild onset of pain or discomfort, we believe. Ask patients with severe onsets when they last felt perfectly well instead of asking them when they first took sick, and numbers of them will recall mild pain (or "constipated discomfort," as one patient told us) persisting for some hours or days prior to the onset of the acute localizing seizure.

Older authors were inclined to dismiss what we call the early stage as a relatively unimportant, prodromal stage, of little significance. Probably they saw most of their patients in the stage of localization, as we may judge by the advice of McBurney,[16] who in 1889 advised delay in operating as a rule until the fifth day of illness.

2. *Enteritis.*—Enteritis began mildly in the patients in cases 3 and 5 of this series. It began in "sudden, explosive" fashion, as described by Quigley and Contratto,[12] in the patient in case 7.

DIARRHEA IN ACUTE APPENDICITIS

The following points have been made in this presentation.

1. Diarrhea makes the differential diagnosis of appendicitis from enteritis difficult.

2. The patient's pain should be analyzed subjectively to determine (*a*) whether pain is associated with bowel urge or not and (*b*) how diarrhea affects the pain.

3. Failure thus to analyze symptoms subjectively can delay diagnosis dangerously (case 1).

4. The early stage of appendicitis should be distinguished carefully from the stage of localization, both from the pathologic (Wangensteen [4] and Wilkie [3]) and from the chronologic viewpoint.

5. Character and chronology of pain (see charts 1 to 7) should be determined.

The following questions have been raised in the presentation.

1. What effect on pain has diarrhea, defecation and passing gas?

2. Which predominates, the bowel urge or the bowel output?

3. Which predominates, the downward urge to defecate or the upward urge to vomit?

4. What are the answers to questions 1 to 3 in the early stage and in the stage of localization?

NOTE ON CONSTIPATION IN ACUTE APPENDICITIS

First, analyze the patient's "constipated discomfort" from the subjective viewpoint, as suggested. If it is desirable, ask him the following

16. McBurney, C., in Kelly, H. A., and Hurdon, E.: The Vermiform Appendix and Its Diseases, Philadelphia, W. B. Saunders Company, 1905.

three questions. If the three questions are answered as indicated, acute appendicitis is strongly to be suspected.[17]

1. At onset (that is, during the early stage only), did you feel as if something was stopped up inside you? Most patients with acute appendicitis answer, "Yes"; some answer, "No."

2. At onset, did you feel as if passing gas or defecating might relieve your discomfort or pain? Patients with acute appendicitis answer this question, "Yes."

3. At onset, if you could pass gas or defecate, did this relieve your discomfort or pain completely? Patients with acute appendicitis answer, "No."

SUMMARY AND CONCLUSIONS

Careful analysis of the early history helps to differentiate acute appendicitis from enteritis, for the physical and the laboratory findings at times may be identical.,

The character of the early pain differs in the two diseases.

In acute appendicitis the early pain persists, often for many hours, sometimes for days.

In enteritis, the pain is intermittent. Individual pains remit completely after lasting a few minutes only. The whole attack rarely lasts over twelve hours.

Pain which persists longer than twelve hours should be regarded as indicative of acute appendicitis unless proved otherwise.

Pain early in acute appendicitis and in enteritis is associated with bowel urge.

Pain during the early stage of acute appendicitis persists despite diarrhea, defecation or passage of gas.

Pain in enteritis is completely if temporarily relieved by defecation or by diarrhea.

In early acute appendicitis, the bowel urge exceeds the bowel output. In enteritis the reverse may be true.

In early acute appendicitis, the downward urge to defecate exceeds the upward urge to vomit.

Vomiting is relatively rarer in early acute appendicitis than in enteritis.

Our discussion concerns chiefly the early stage of acute appendicitis. During the later stage of localization, tenderness increasing near

17. Keyes.[1] Homans.[10]

McBurney's point is commoner in acute appendicitis than in enteritis. Muscle spasm, rebound and rectal tenderness and other signs of peritoneal irritation occur commonly in acute appendicitis and rarely in enteritis.

Diagnosis of acute appendicitis may be made in the early stage by criteria in tables 1 and 2. In differential diagnosis the history is the most important guide; physical and laboratory findings, though less important, are not to be neglected.

TREATMENT OF FRACTURES OF THE CARPAL SCAPHOID

A Report of Sixty-Four Cases

MAJOR DAVID SASHIN

MEDICAL CORPS, ARMY OF THE UNITED STATES

FRACTURE of the carpal scaphoid is a common finding in military practice. But, unlike fractures of the other bones, the clinical picture usually presents no pronounced objective findings, and unless the examiner tests for local tenderness, restriction of dorsiflexion of the wrist and weakness of the hand the diagnosis is overlooked. Often many months may pass before roentgenograms are taken and the fracture discovered. In fact, in some cases roentgenograms taken in the conventional anteroposterior and lateral views may not disclose the fracture, with the result that the actual pathologic condition is not recognized and is improperly treated.[1] From the standpoint of time lost and persistence of symptoms, the fractured carpal scaphoid must be considered a major disability, comparable in many respects to fractures of the neck of the femur.

The prolonged disability usually associated with fractures of the carpal scaphoid is due chiefly to three factors: first, failure to recognize the fracture soon after the injury; second, inadequate treatment, both as to type of immobilization and as to length of the period of fixation, and, third, disturbance of the circulation in the proximal fragment, with resulting delay in union. Failure to diagnose the condition early is common and has been noted by nearly all writers on this subject. Dickison and Shannon[2] stated that the primary problem is early diagnosis and that when seen early and properly treated the fracture will almost invariably unite. In like manner, Soto-Hall and Haldeman[3] claimed that early diagnosis is absolutely imperative and failure to institute treatment immediately is one of the main factors in the production of nonunion. Watson-Jones[4] felt that in every case giving a history of

From the Orthopedic Section, Oliver General Hospital, Augusta, Ga.

1. Murray, G.: Bone-Graft for Non-Union of the Carpal Scaphoid, Brit. J. Surg. **22**:63 (July) 1934.

2. Dickison, J. C., and Shannon, J. G.: Fractures of the Carpal Scaphoid in Canadian Army: A Review and Commentary, Surg., Gynec. & Obst. **79**:225 (Sept.) 1944.

3. Soto-Hall, R., and Haldeman, K. O.: Treatment of Fractures of the Carpal Scaphoid, J. Bone & Joint Surg. **16**:822 (Oct.) 1934.

4. Watson-Jones, R.: Fractures and Joint Injuries, ed. 3, Edinburgh, E. & S. Livingstone, 1944.

injury to the wrist in which tenderness is present over the radial aspect a diagnosis of fracture of the carpal scaphoid bone must be considered unless repeated roentgenograms prove otherwise.

The main point in the treatment of fresh fractures is immediate and complete plaster immobilization of the wrist for about three months or until there is evidence of bone healing. When this is carried out, the fractured scaphoid will unite in the vast majority of cases. The failures result because of a lack of appreciation by many physicians of the importance of immediate and prolonged immobilization. The question is frequently asked: Why is it necessary to immobilize the wrist for several months in fractures of the scaphoid when only three weeks suffice for fractures of the bones of the hand and the forearm? The length of the period of fixation is dependent on the time it takes for the bone to heal. Bones of the cancellous type heal more slowly than long bones, and in the cases of fracture across the waist or proximal pole of the scaphoid bone union is further delayed by the intra-articular nature of the fracture and, in about one third of the cases, by a disturbance of the circulation to the proximal fragment.

Fractures of the scaphoid may occur at three different levels: at the tubercle, at the waist and at the proximal pole. Fractures of the tubercle occur in only a small percentage of cases. The fracture is extra-articular; there are strong ligamentous attachments to it, and the blood supply is ample. Bony union takes place early, and the wrist is immobilized for a period of only three weeks. Fractures across the waist, or constricted midportion, of the bone are the commonest. As in fractures of the proximal pole, they are intra-articular; they heal slowly, and in an appreciable percentage of cases there is an impairment of the blood supply to the proximal fragment. Firm, uninterrupted plaster immobilization is essential for a period of three months or longer, until there is a disappearance of the fracture line as seen by roentgenologic examination.

Dickison and Shannon,[2] in a review of 257 cases of fractured carpal scaphoids, found the tubercle involved in 23 cases, or in 10 per cent, the waist in 196 cases, or 75 per cent, and the proximal pole in 38 cases, or 15 per cent. The average period of immobilization in their 114 cases of fractures of the waist which united was twelve and one-half weeks. In only 10 per cent was there evidence of healing at the end of two months; in 48 per cent, the bone healed in three months, in 74 per cent in four months and in 82 per cent in five months.

Obletz and Halbstein,[5] in a study of the blood supply of two hundred and ninety-seven carpal scaphoids which had been removed from cadavers, found that in 13 per cent of the bones there were no arterial fora-

5. Obletz, B. E., and Halbstein, B. M.: Non-Union of Fractures of the Carpal Navicular, J. Bone & Joint Surg. **20**:424 (April) 1938.

mens proximal to the waist and in 20 per cent there was a single small arterial foramen at the waist or proximal to it. Since most fractures occur in this region, the circulation of the bone proximal to it would be completely interrupted in 13 per cent of the cases and impaired in another 20 per cent. Thus in about one third of the cases a disturbance in the blood supply of the proximal fragment occurs, which delays union and if not properly treated will result in nonunion. Johnson,[6] in a study of the healing processes in injuries of the carpal scaphoid in dogs, found a lack of periosteal callus a large factor in delay of bony union.

It is now well recognized that in fractures across the waist and the proximal pole of the scaphoid union is delayed and immobilization must be maintained until bone healing is noted by roentgenologic examination. Nonunion usually results when the fracture is not recognized early and when immobilization is not complete or is not maintained for a long enough period. Thorndike and Garrey[7] reported that of 17 cases observed in a college clinic 11 cases, or 65 per cent, were those of old, previously unrecognized fractures of the scaphoid. Obletz and Halbstein,[5] in a review of 30 cases of nonunion, found that in 17 the fracture was not recognized and in the others the treatments given were inadequate. Henry[8] found an incidence of 25 per cent of nonunion in a series of 12 cases seen in an industrial practice and in 32 per cent of 22 cases seen in a large receiving and embarkation base.

There can be little doubt that the high incidence of nonunion with resulting long disability is in large measure a reflection of the type and the character of medical service rendered. It is, therefore, in the hope of improving the understanding and treatment of this fracture that this paper is presented.

MAIN FACTORS IN THE MANAGEMENT OF THE FRACTURED SCAPHOID

1. Early Diagnosis.—A thorough clinical examination of the wrist should be made in all cases. Restriction of motion, especially of dorsiflexion, localized tenderness and weakness of the hand, are to be noted. Roentgenograms are to be taken in all cases in which there is a history of injury and in all others in which symptoms persist and no improvement has occurred after a week to ten days of treatment. When one considers the large number of fractures that have been missed because roentgenograms were not taken, it seems imperative to adopt a policy of roentgenologically examining all patients giving a history of a fall on the outstretched hand or any other injury to the wrist joint. The roentgeno-

6. Johnson, R. W., Jr.: A Study of the Healing Processes in Injuries to the Carpal Scaphoid, J. Bone & Joint Surg. **9**:482 (July) 1927.

7. Thorndike, A., Jr., and Garrey, W. E.: Fractures of the Carpal Scaphoid, New England J. Med. **222**:827 (May 16) 1940.

8. Henry, M. G.: The Fractured Carpal Scaphoid in Industry and in the Military Service, Mil. Surgeon **95**:199 (Sept.) 1944.

grams should be taken in three views: anteroposterior, lateral and oblique. For the anteroposterior view, it is necessary to hold the hand in ulnar deviation to get a complete view of the scaphoid. In some cases the fracture may not be seen on a roentgenogram; however, if symptoms persist new roentgenograms are to be taken at the end of two to three weeks.

2. Closed Reduction of Fracture and Complete Immobilization in a Plaster of Paris Cast.—The fracture should be reduced with the patient under anesthesia if any displacement or separation of the fragment is present. The cast should extend from just below the elbow to the interphalangeal joint of the thumb and to the metacarpophalangeal joints of the other fingers. The wrist should be maintained in moderate dorsiflexion and radial deviation and the thumb in slight abduction. This position will fix the scaphoid and thumb and yet provide ample and complete freedom of movement of the other fingers. Check-up roentgenograms should be taken at monthly intervals, and at the end of three months the cast is bivalved and roentgenograms taken while the position of the wrist is held. If insufficient healing of the bone is noted, a new cast is applied and left on for another month. Usually three months of immobilization is sufficient time to allow for union to take place. In cases in which no signs of bone healing can be discerned after three to four months of fixation—and this may occur in fractures across the waist and the proximal third of the bone—operation is indicated.

3. Open Operation.—In fresh fractures, operation should be performed only when the scaphoid is badly comminuted, with the fragments displaced, and when attempts at closed reduction have failed. Operation in this instance is resorted to in order to prevent the development of a painful traumatic arthritis of the wrist. The vast majority of patients that come to operation are those with ununited fractures that have been overlooked and treated for months as mild sprains or when seen early were inadequately immobilized and treated by strapping and physical therapy. In these cases further conservative therapy would offer little hope of obtaining bony union. The main criterion for operation is nonunion associated with persistence of clinical symptoms and with the patient unable to perform his regular duties. Every patient considered for operation must be carefully scrutinized so as to eliminate the psychoneurotic patients and those harboring a desire to avoid duty. The temptation to play sick is inviting to some, and unless this is guarded against the best operation may result in clinical failure.

There are many operative procedures that have been used. The commoner ones are the following: total and partial excision of the scaphoid, drilling of the bone and bone graft.

The total excision of the scaphoid has been advocated by some surgeons. Davidson and Horwitz [9] recommended the operation in all badly comminuted fractures of the scaphoid and in some cases of nonunion with persistent disability that have been given a fair trial of conservative therapy. Henry,[8] in a recent paper, advised the complete excision of the bone in fractures through the middle and inner third when there is any degree of displacement. Most surgeons, however, would disagree with this view. The main objection to the operation is that it tends to disorganize the general alinement and architecture of the carpal bones. In my experience, this operation should be employed only in pronounced comminuted fractures of the scaphoid in order to prevent the development of traumatic arthritis of the wrist.

Partial excision of the small, ununited proximal fragment is indicated in cases in which the fracture is across the proximal third of the bone and when it is displaced or separated and is small. This procedure is also used when the proximal fragment has undergone avascular necrosis, as noted on the roentgenogram by the increased density of the bone. In other cases, the operation may be employed when symptoms persist with no evidence of bony union after a period of three to four months of plaster immobilization and when the proximal fragment is too small for drilling or for the insertion of a bone peg. After the excision of the small proximal fragment, the general position and alinement of the carpal bones are not disturbed. Motion of the wrist is started shortly after the operation. In selective cases the operation is of distinct value. This paper will present the case histories of patients on whom the operation has been performed.

Drilling of the fractured bone is advocated by many surgeons for nonunion. According to Obletz and Halbstein,[5] drilling, when followed by adequate immobilization, is the treatment of choice for ununited fractures of the carpal scaphoid. Soto-Hall and Haldeman [3] advised this procedure, and Rothberg [10] felt that firm bone union may be expected from this simple method. Bunnell [11] found that drilling often succeeds in restoration of circulation and leads to union. Watson-Jones [4] stated that in the treatment of fractures of the carpal scaphoid with established nonunion immobilization alone will not succeed and that it must be preceded by either multiple drilling or bone grafting to obtain union. In my opinion, drilling is of value in cases in which the fractured fragments

9. Davidson, A. J., and Horwitz, M. T.: An Evaluation of Excision in the Treatment of Ununited Fracture of the Carpal Scaphoid Bone, Ann. Surg. **108:** 291 (Aug.) 1938.

10. Rothberg, A. S.: Ununited Fractures of the Carpal Scaphoid, Am. J. Surg. **56:**611 (June) 1942.

11. Bunnell, S.: Surgery of the Hand, Philadelphia, J. B. Lippincott Company, 1944.

are in apposition and there is no displacement or bone absorption of the fragments. The operation is simple, is easily carried out and when followed by adequate immobilization will often result in bone union. The main purpose of drilling is to break across the sclerosed bone at the fractured ends and permit the ingrowth of vascular channels into the proximal fragment, with resultant healing of the fracture.

The bone graft operation is indicated in cases of nonunion associated with symptoms and prolonged disability. I have used an autogenous tibial bone peg, with satisfactory results. The graft has the added advantage over drilling in that it insures bony continuity by internal fixation of the fragments and provides a local store of calcium on which the body may draw. The operation offers the best means of obtaining union in old, ununited fractures. Although some physicians are opposed to the bone graft because it is a highly technical procedure, the operation is not difficult, but it should be attempted only by a surgeon who is familiar with the use of a motor saw. Check-up roentgenograms should be taken during the operation to make sure that the graft is in the exact position.

The operation consists in removing a small graft from the tibia and converting it into a rounded peg. This is then inserted into a previously prepared drill hole across the fracture line in the scaphoid. The size of the bone peg should correspond to the hole and should fit snugly so as to obtain firm internal fixation of the fragments. I use the Albee bone mill.[12] The wrist is then immobilized in a plaster cast in moderate dorsiflexion and radial deviation, and the cast should extend from the upper third of the forearm to the interphalangeal joint of the thumb and to the metacarpophalangeal joints of the other fingers. The plaster is left on for three months or until there is evidence of bone healing on roentgenologic examination.

CLINICAL DATA

From January 1943 to April 1945, 64 patients with fracture of the carpal scaphoid were admitted to the Oliver General Hospital. The patients came from station hospitals serving nearby training camps and from hospitals overseas. The average age was 26; the youngest patient was 19 and the oldest 37 years. In this series, only 39 patients, or 61 per cent, received adequate plaster immobilization of the wrist shortly after the injury. In 3 cases a splint was applied and left on for three to six weeks, while in 5 others the wrist was strapped with adhesive tape or was given physical therapy. Seventeen patients received no immediate treatment; their fractures were overlooked, and diagnoses were not made until months or years later.

12. Albee, F. H., and Kushner, A.: Bone Graft Surgery in Disease, Injury, and Deformity, New York, D. Appleton-Century Company, Inc., 1940.

Of the 39 patients receiving proper immobilization, the fracture united in 34, or 87 per cent. The average length of fixation was three months. In 5 patients nonunion developed and required open operation. In 2 of these the small proximal fragments were excised, and in 1 the fragments were drilled; in 2 cases bone grafts were used. Of the 25 patients not receiving adequate immediate fixation, nonunion developed in 24, or 96 per cent (table 1).

From the figures given, it is apparent that early, complete and prolonged plaster immobilization of the fresh fractured carpal scaphoid is most important and is the key to the successful treatment of this fracture. Fixation should be maintained until there is distinct evidence of union by roentgenologic examination as seen by the disappearance of the fracture line and uniform density of the bone structure.

Nonunion was found in 29, or 45.3 per cent of the cases. Twenty patients were operated on, 17 by me and 3 by others at different hospitals. Nine patients received no specific treatment. Of the latter, 3

TABLE 1.—*Analysis of Sixty-Four Cases*

	Cases		Cases of Bony Union		Cases of Nonunion	
	No.	%	No.	%	No.	%
Plaster immobilization after injury, 2 to 4 months	39	61	34	87	5	13
Splint, 3 to 6 weeks	3	4.7	1	33	2	66
Adhesive strapping or physical therapy.	5	7.8	0	0	5	100
No immediate treatment; fracture not diagnosed until 3 months later	17	26.5	0	0	17	100
Total	64	100	35	54.7	29	45.3

patients sustained this injury prior to induction into the service, 1 having received it sixteen years ago. The symptoms and restriction of wrist motion were mild. In 2 patients the fractured scaphoid was first discovered during a routine general physical examination. They had no recollection of any injury to the wrist. Roentgenograms disclosed old nonunion of the carpal scaphoid. There were no symptoms and only mild objective findings. Both patients were in the hospital on account of other injuries. In 1 case because of the presence of a duodenal ulcer and in another because of psychoneurosis, operation was not deemed advisable. One patient was transferred to another hospital and later returned to duty. Of the 9 patients in the nonoperative cases, 1 was returned to full general duty, 1 was discharged from the service on account of renal glycosuria and 7 were reclassified to limited duty.

In the operative group, the procedures employed were excision of the proximal fragment, drilling of the bone and bone graft. Of the 3 patients operated on elsewhere, drilling was employed in 1 and bone grafts in 2. Of the 17 patients operated on here, excision was per-

formed in 6, drilling in 3 and bone grafts in 10. Two of the latter were later reoperated on and the proximal fragment excised. The average period from date of injury to operation was fourteen months.

REPORT OF CASES

Partial Excision of the Carpal Scaphoid Bone.—The first 6 cases are typical of this group.

CASE 1.—The patient, aged 25, injured his wrist in February 1943, when he fell on an extended arm, bending his wrist backward. The condition was considered a sprain, and when the symptoms subsided he was sent overseas with his outfit. Three months after his arrival, because of pain and stiffness in dorsiflexion, the first roentgenograms were taken which revealed a fracture of the carpal scaphoid. A cast was applied and left on for two months, without any improvement.

Fig. 1 (case 1).—*A*, roentgenogram taken twenty-two months after injury, showing nonunion fracture of the proximal pole of the scaphoid. *B*, ten days after excision of the small proximal fragment. The general alinement of the proximal carpal bones has not been disturbed.

On examination, there were localized tenderness and pain on dorsiflexion of the wrist. Roentgenograms revealed a fracture of the proximal pole of the

scaphoid (fig. 1*A*). On Dec. 4, 1944, twenty-two months after his injury, an operation was performed and a small, loose, triangular fragment excised. The fractured end was found to be smooth and loosely connected by fibrous tissue. Microscopic section disclosed avascular necrosis of the bone. Roentgenograms taken on December 14 showed the small fragment removed and the general position and alinement of the proximal carpal bones unchanged and in normal relationship to the radius (fig. 1*B*).

Case 2.—The patient, aged 31, injured his wrist on Sept. 5, 1944, when thrown approximately 30 feet (9.1 meters) as a result of a nearby shell explosion. He did not apply for treatment until two months later, when roentgenograms were taken and a fracture of the scaphoid disclosed. A plaster cast was then applied and left on for four months, but without relief of the symptoms.

Fig. 2 (case 2).—Roentgenogram taken April 2, 1945, seven months after injury, showing nonunion fracture across the proximal pole. The small fragment is slightly displaced and presents a dense appearance indicative of avascular necrosis of the bone.

On examination, motion of the wrist was moderately restricted and painful, especially in dorsiflexion. There was tenderness over the carpal scaphoid. Roentgenograms taken April 2 disclosed an old fracture of the proximal pole of the scaphoid with nonunion. The upper fragment was slightly displaced and appeared denser then the rest of the bone (fig. 2). On April 5 the proximal fragment was excised and early motion started.

Case 3.—The patient, aged 33, injured his left wrist in September 1943, when his truck collided with another car, as a result of which he sustained a fracture of the semilunar and scaphoid bones. The wrist was immobilized in a number of plaster casts for about six and one-half months, and the patient was then returned

to duty. In December 1944, because of complaints of pain and stiffness in the wrist, he was admitted to another hospital, and after receiving physical therapy he was sent back to duty. However, two weeks later he was readmitted and then transferred to this hospital for treatment.

On examination, all motion of the wrist was restricted and painful. There was tenderness over the scaphoid. Roentgenograms disclosed an old fracture of the proximal pole of the scaphoid with several ununited, loose fragments and with evidence of early traumatic arthritis (fig. 3*A*). On April 12 he was operated on, and three small, irregular, bony fragments, loosely attached to the scaphoid, were excised (fig. 3*B*). On the next day, active motion was started and the patient was instructed to move the wrist.

In the following case, avascular necrosis of the proximal fragment developed as a result of severe injury to the wrist.

CASE 4.—The patient, aged 21, sustained an injury to his left wrist when he was thrown from a jeep. Roentgenograms were immediately taken which dis-

Fig. 3 (case 3).—*A*, roentgenogram taken March 3, 1945, showing an old fracture of the proximal pole of the scaphoid. The upper fragment is irregular and has a dense appearance. At operation three small, loose, dense fragments were found in this area and were removed. The wrist joint is narrowed, and there is some sclerosis of the articulating surface of the radius indicative of early traumatic arthritis. *B*, postoperative view. The loose fragments were completely excised.

closed a fracture of the lower end of the left radius and ulna, a fracture of the scaphoid and a dislocation of the semilunar bone. An attempt was made at the station hospital to reduce the fractures, but only the dislocated bone was replaced and the patient was transferred to this hospital for further treatment (fig. 4*A*).

On examination, motion of the wrist was restricted and painful. There were moderate swelling and tenderness of the wrist joint. With the patient under general anesthesia, the fractured scaphoid was reduced (fig. 4*B*) and a plaster cast applied. Five weeks later, roentgenograms were taken which disclosed the proximal fragment dense and sclerotic, indicative of avascular necrosis of the bone (fig. 4*C*). In view of this finding, the proximal fragment was excised (fig. 4*D*). The pathologic report was avascular necrosis of the bone.

CASE 5.—The patient, aged 28, injured his left wrist on June 3, 1943, when his hand was caught between a gun and the side of a tank. His condition was treated as a sprain. However, because of continued symptoms, roentgenograms were taken, which disclosed a fracture of the proximal pole of the scaphoid (fig. 5*A*).

On examination, motion of the wrist was restricted and painful, particularly in dorsiflexion. Tenderness was localized over the scaphoid bone. Because of

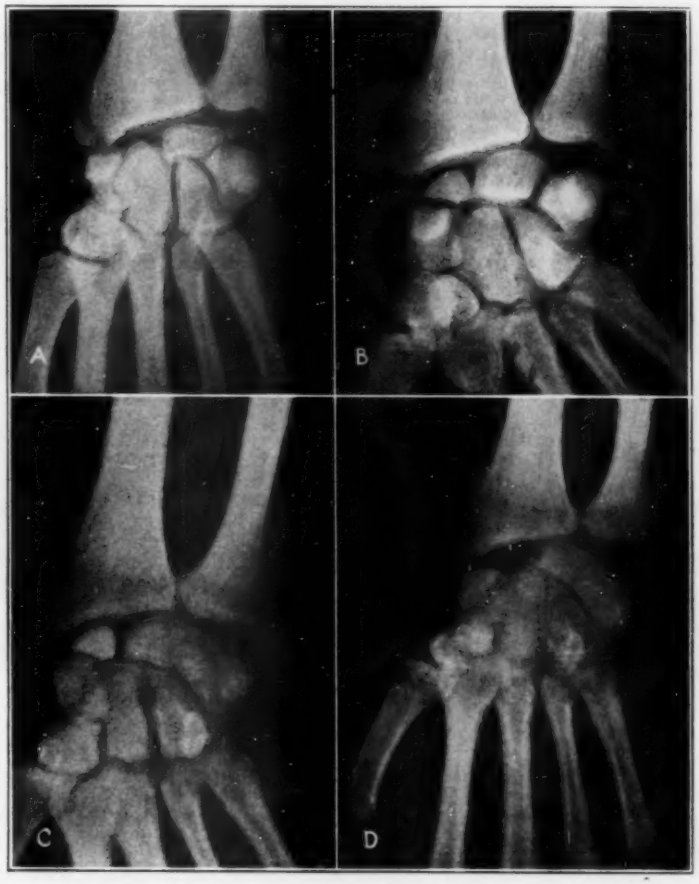

Fig. 4 (case 4).—*A*, roentgenogram taken eleven days after injury, showing fracture across the proximal pole with dislocation of the upper fragment. There is also a fracture of the lower outer end of the radius and a fracture of the styloid process of the ulna. *B*, reduction of the fractured scaphoid. *C*, on October 16, seven weeks after the injury, the proximal fragment is dense and sclerotic, indicative of avascular necrosis of the bone. *D*, the proximal fragment excised and motion started.

the persistence of symptoms and disability with the presence of nonunion, a bone peg was inserted. The wrist was immobilized for four months, and then physical therapy was started. However, the patient still complained of pain.

Roentgenograms showed the bone peg extending beyond the articular surface of the bone, with no evidence of union. The proximal fragment was therefore excised (fig. 5*B*).

Case 6.—The patient, aged 29, injured his right wrist in July 1942, when he fell off a truck. It was considered a sprain, and after a week of rest he returned to duty. In June 1944 he again injured his wrist, and roentgenograms disclosed a fracture of the scaphoid. A cast was applied and left on for a month. He was then returned to duty but was unable to continue his work.

On examination, there were tenderness and moderate restriction of motion of the wrist. Roentgenograms disclosed an old, ununited fracture of the scaphoid. On Dec. 5, 1944 a bone peg was inserted, and check-up roentgenograms revealed satisfactory position. There was no postoperative reaction, and two weeks later the patient was given a furlough. While home, he became intoxicated and removed the cast. When he returned, he had on a loose, short cast, which had been

Fig. 5 (case 5).—*A*, roentgenogram showing old fracture across the proximal pole of the scaphoid. *B*, after excision of the small proximal fragment.

applied the day before at a dispensary. Roentgenograms disclosed the bone peg displaced in the joint. An excision of the proximal fragment was performed and active motion started.

Drilling Operation.—The following case is typical of the group.

Case 7.—A private, aged 29, while finishing his training in Northern Ireland, fell on his outstretched hand and injured the right wrist. Two days later, roentgenograms were taken which revealed a fracture of the scaphoid. His wrist was not immobilized, and shortly thereafter he was sent with his outfit to France. While in action, he received a rifle bullet injury, sustaining a compound comminuted fracture of the upper third of the ulna. When seen here, his chief complaint was pain and stiffness of the right wrist.

On examination, motion of the wrist was considerably restricted in volar flexion and dorsiflexion. Side bending gave rise to pain, and there was tender-

ness over the scaphoid. The fractured ulna was firmly united. Roentgenograms disclosed nonunion of the scaphoid and a healed comminuted fracture of the ulna. Because of the persistence of symptoms a bone peg procedure was considered, but at operation eight months after the injury the fractured scaphoid bone was found to be in excellent position and in close contact and drilling was done instead. As the drill passed acoss the fractured ends of the bone an increase in resistance was felt.

Bone Graft Operation.—Typical of this group are the following cases.

CASE 10.—A private first class, aged 24, injured his wrist in January 1943, when he fell on the ice while running to catch a bus. He had another injury

Fig. 6 (case 10).—Roentgenogram showing old fracture across the waist of the scaphoid. The fracture ends appear rounded and show cystic changes.

on Dec. 3, 1943, when he fell backward, landing on his right hand. Roentgenograms were taken which disclosed a fracture of the carpal scaphoid.

On examination, motion of the wrist was considerably restricted. There was tenderness over the scaphoid and weakness of the hand. Roentgenograms disclosed a transverse fracture through the scaphoid, with slight separation of the fragments. The fracture edges were rounded and showed cystic changes (fig. 6). On Jan. 16, 1944, twelve months after the original injury, a tibial bone peg was inserted. The wrist was immobilized in a plaster cast for three months, and an aluminum cock-up splint was then applied and left on for another month. Physical therapy was begun after the removal of the casts. Roentgenograms showed the bone graft in place (fig. 7). The postoperative course was uneventful, and the patient was discharged to full duty.

CASE 11.—A corporal, aged 24, injured his right hand in July 1943 as a result of recoil from a gun breech while he was stationed in Panama. He had pain and swelling of the wrist, but at the time of injury he was stationed in the jungle and had no medical treatment. Three months later he was examined

Fig. 7 (case 10).—Four months after operation. The bone graft is in place and the fracture line indistinct.

Fig. 8 (case 11).—Roentgenograms taken March 24, 1944, eight and a half months after the injury, shows fracture across the proximal pole of the scaphoid. The fracture line is distinct.

by a medical officer, but no roentgenograms were taken. Because of persistent pain in the wrist and weakness of the hand, he was admitted to the station hospital, where roentgenograms were taken which disclosed a fracture of the scaphoid (fig. 8).

On examination, there were localized tenderness and weakness of the grip of the right hand. A tibial bone peg operation was performed on April 25, 1944, ten months after the injury. At operation the bone fragments were movable on slight pressure. Roentgenograms taken show the bone peg in place (fig. 9 *A*). On July 21 the cast was removed, and roentgenograms taken disclosed that the fracture line was indistinct and union was present (fig. 9 *B*). Physical therapy was started, and all motions of the wrist returned to normal. He made a complete recovery and was returned to full duty.

CASE 16.—The patient, aged 29, injured his hand during a parachute jump in October 1942. A plaster cast was applied and left on for five months, and the patient was then returned to duty. In September 1944 he again injured his

Fig. 9 (case 11).—*A*, the bone peg is in place. *B*, on July 25, 1944, three months following operation, there is firm bony union of fracture. The fracture line is not seen.

wrist. Roentgenologic examination disclosed nonunion of the carpal scaphoid and a fresh fracture of the styloid process of the ulna.

On examination, there was restriction of motion of the wrist and tenderness over the scaphoid. A roentgenogram taken February 10 disclosed an old, ununited fracture across the waist of the scaphoid. There was a small fragment lateral to the main fracture line (fig. 10*A*). On March 13 a tibial bone peg was inserted and a cast applied (fig. 10*B*).

CASE 17.—The patient, aged 35, injured his right wrist while in action on July 13, 1944. The wrist was fixed in plaster for about five months. However, he still complained of pain and stiffness and was therefore evacuated to the Zone of the Interior.

On examination, motion of the wrist was greatly restricted. There was tenderness over the scaphoid. Roentgenologic examination disclosed an old fracture of the scaphoid with nonunion (fig. 11 *A*). On April 2 a tibial bone peg operation was performed and a cast was applied (fig. 11*B*).

Fig. 10 (case 16).—*A*, roentgenogram taken Feb. 10, 1945, twenty-nine months after the first injury, discloses an old, ununited fracture across the waist of the scaphoid. There is an increased density of the fractured ends, with a healed small fragment lateral to the main fracture. *B*, bone peg in place and extending across the fracture line. The position and alinement of the bone are good. The plaster cast is applied in slight radial deviation and extends to the interphalangeal joint of the thumb and to the metacarpophalangeal joints of the other fingers.

Fig. 11 (case 17).—*A*, roentgenogram taken Jan. 9, 1945, six months after the injury, discloses an old fracture across the scaphoid, with nonunion. There is slight separation of the fragments. *B*, bone peg in place. Position and alinement of the fragments are good.

COMMENT

Although the number of operative cases is not large, the clinical picture is typical of the general pattern of this fracture. A common finding in the case histories is the failure to diagnose the condition early and to immobilize the wrist adequately. In many cases the condition was considered a mild sprain, and, after the wrist had been strapped with adhesive tape, the patient was returned to duty. As a consequence, nonunion developed, with resulting pain and stiffness. What at first is a simple fracture when improperly managed may result in an incapacitating disability which may require many months to resolve. It is obviously imperative for the physican to become cognizant of this condition, to recognize the pathologic condition early and to firmly immobilize the wrist for about three months if he is to avoid undesirable sequelae.

The presence of nonunion of the scaphoid is not in itself an indication for operation. In 2 of the patients the fracture was accidentally discovered in the course of a routine examination. They had no symptoms and no recollection of any injury to the wrist. The patients were in the hospital on account of other injuries. In several other cases the symptoms and restriction of motion were mild, and the condition had existed for many years without much discomfort. Operation, however, is indicated when symptoms and disability are associated with the nonunion and when the patient is unable to continue with his regular duties.

In such cases I have employed three types of operative procedure. The choice depends on the type, the position and degree of separation and the displacement of the fractures. Excision of the proximal pole is especially indicated when the fragment is small or displaced or when avascular necrosis develops. Drilling across the fractured fragments is of value in cases of nonunion when the fragments are in close contact and in good alinement. The operation is simple and is easily carried out. The bone graft operation should be employed in cases of nonunion across the waist and in cases in which there is separation or displacement of the fragments. The graft provides firm internal fixation of the fractured bone. At first, a large bone peg (Albee peg 2) was used, measuring .238 inches (0.5 cm.); now the small peg (peg 1), .145 inches (0.3 cm.), is mainly used and provides firm fixation with the least destruction of bone substance.

Firm immobilization with plaster is essential following drilling and bone graft operations. This is maintained for about three months or until there is evidence of union by roentgenologic examination. After partial excision of the bone active motion is started twenty-four to forty-eight hours after operation, and in a month the patient is able to return to duty.

There were no postoperative reactions in these cases, and in a few days after operation the patients were up and about. Patients with plaster casts are advised to exercise their fingers, and all the patients are urged to go to the occupational therapy department, where they are assigned to special projects to facilitate movement of the finger joints. One of the patients was a weaver, and with the cast on he was able to make rugs and teach others how to work on the loom. In civilian practice, this group of patients could be discharged from the hospital in a few days after operation and would be able to do light work until the casts were removed.

In selection of patients for operation, an attempt should be made to rule out patients showing psychoneurotic traits or harboring a desire to avoid going back to duty. Unless this is done, the best operative result may often prove unavailing and not alleviate the patient's complaints. The military patient has the advantage over the civilian patient in that he continues to draw his full pay and enjoys all the rights and privileges associated with his rank. Life in a hospital is pleasant and comfortable as compared with life in the field. The hazards and the dangers of battle conditions are so vividly remembered by some patients that their desire to avoid another such experience may hamper and delay their complete recovery. In 3 patients operated on at other hospitals the roentgenograms revealed complete bony union of the fractured scaphoid, and on examination there was only slight limitation of motion of the wrist. Yet, despite the evident good result, they still complained of pain and were referred to this hospital for further treatment. After a short stay here, they were returned to full duty.

In 1 of my own patients (case 13), a bone graft operation was performed, and after the plaster was removed he was referred to a convalescent hospital prior to his return to duty. While at that hospital he continued to complain of pain and stiffness in the wrist and, as a result, was sent back to me for further treatment. Roentgenograms taken disclosed complete and firm bony union of the fractured scaphoid. Because of the restriction of motion of the wrist, he was taken to the operating room and, with the patient under general anesthesia, the wrist was manipulated. The range of motion was good, with only a slight limitation in dorsiflexion and volar flexion. His symptoms were considered largely functional. He was encouraged to move his wrist constantly, and after a short stay he returned to limited duty.

Because of the presence of associated injuries, diseases or psychogenic factors, the final result cannot be measured entirely by the disposition of the case but, rather, must be determined by roentgenologic examination, by objective findings, such as range of motion of the wrist, swelling, tenderness and weakness of the grip, and by the subjective

complaints. In the cases of partial excision of the bone, the results in 3 (cases 1, 2 and 4) must be regarded at good, in 1 (case 3) as undetermined, as the patient is still under treatment, and in 2 (cases 5 and 6) as fair (table 2). In the last group, 1 patient returned to full duty, but in a follow-up letter a year later he still complained of pain; the other patient was given limited duty and assigned to this hospital. In case 3, the roentgenograms disclosed a healed fracture of the semilunar and a fracture of the proximal pole of the scaphoid, with three small ununited bone fragments and with evidence of traumatic arthritis of

TABLE 2.—*Analysis of Seventeen Operative Cases*

Case	Age of Patient, Yr.	Date of Injury	Immediate Treatment	Operation	Date of Operation	Period Injury to Operation, Mo.	Clinical Result: Union Shown by Roentgenogram*	Clinical Result: Objective Findings	Clinical Result: Subjective Findings
1	25	2/43	Strapping	Excision	12/ 4/44	22	..	Good	Good
2	31	9/5/44	None	Excision	4/ 5/45	7	..	Good	Good
3	33	9/43	Plaster cast	Excision	4/13/45	19	..	Fair	Poor
4	21	8/30/44	Plaster cast	Excision	10/18/44	7 weeks	..	Good	Good
5	28	6/ 3/43	Strapping	Bone graft Excision	2/17/44 7/ 6/44	8½	—	Good	Fair
6	29	7/43	None	Bone graft Excision	12/ 8/44 3/ 5/45	28	—	Fair	Good
7	29	1/44	None	Drilling	2/ 6/45	8	++	Good	Good
8	23	9/44	Splint	Drilling	4/19/45	7	++	Good	Good
9	31	12/44	None	Drilling	4/20/45	5	Undetermined; patient under treatment		
10	24	1/45	None	Bone graft	1/27/44	12	+	Good	Good
11	23	2/20/43	Strapping	Bone graft	2/29/44	12	+	Good	Good
12	24	7/43	None	Bone graft	4/25/44	9	++	Good	Good
13	27	5/5/43	Splint	Bone graft	6/ 1/44	13	++	Good	Fair
14	27	11/41	None	Bone graft	6/30/44	31	+	Good	Good
15	33	10/42	Splint	Bone graft	7/ 3/44	21	+	Fair	Fair
16	29	10/42	Plaster cast	Bone graft	3/13/45	30	Undetermined; patient under treatment		
17	35	7/13/44	Plaster cast	Bone graft	4/ 2/45	9	Undetermined; patient under treatment		

* Explanation of symbols: ++ = firm bony union, with disappearance of fracture line; + = union, with fracture line and bone graft still visible, and — = no union.

the wrist joint. Fusion of the wrist was considered, but excision of the loose fragments was performed in the hope that by removal of the irritant factors the arthritic symptoms would clear up. The result in this case must be considered undetermined and possibly poor.

Of the 3 patients that had drilling operations, the results in 2 cases (cases 7 and 8) are good and in 1 uncertain. In the latter, the patient was only recently operated on. In the series of bone grafts, the results in 4 cases (cases 10, 11, 12 and 14) are good and the patients were returned to full duty. In 2 (cases 13 and 15), the results are fair; objectively they are good, but subjectively the patients continued to

complain of pain. They were returned to limited duty. Two patients (cases 16 and 17) are still in the hospital, and the postoperative roentgenograms (fig. 8*B* and 9*B*) show the graft in place and in good position.

SUMMARY

1. Fracture of the carpal scaphoid bone is a common finding in military practice. From the standpoint of time lost, persistence of symptoms and disability, the fractured carpal scaphoid bone is comparable in many respects to fractures of the neck of the femur.

2. The prolonged disability frequently associated with fractures of the scaphoid is due to three main factors: first, failure to recognize the fracture soon after injury; second, inadequate treatment, both as to type of immobilization and as to period of fixation, and, third, disturbance of the circulation to the proximal fragment, with resulting delay in union.

3. Early diagnosis is most important. Roentgenograms are to be taken in all cases in which there is a history of a fall on the outstretched hand or any other injury to the wrist and in all others in which symptoms persist and no improvement has occurred after ten days of treatment. Roentgenograms should be taken in three views: anteroposterior, lateral and oblique. In some cases, the fracture may not be seen on roentgenologic examination; however, if symptoms persist, new roentgenograms are to be taken at the end of two or three weeks.

4. The main point in the treatment of fresh fractures is immediate and complete plaster immobilization of the wrist for about three months or until there is evidence of bone healing by roentgenologic examination.

5. From January 1943 to April 1945, 64 patients with fracture of the carpal scaphoid were admitted to this hospital. Only 39 patients, or 61 per cent, had received proper plaster immobilization of the wrist shortly after injury. In this group 34, or 87 per cent, of the fractures united. The average period of fixation was three months. Of the 25 patients not receiving immediate adequate treatment, nonunion developed in 96 per cent.

6. Nonunion was found in 29, or 45.3 per cent, of the total 64 cases in the series. Twenty patients were operated on, 17 by me and 3 by others at different hospitals. The operative procedures employed were excision of the proximal fragment, drilling of the bone and bone graft.

7. Firm bony union was obtained in 4 cases. In 4 others, there was roentgenologic evidence of union but the fracture line was still visible four to six months after operation. In 2, there was no union following bone graft and an excision of the proximal fragment was performed. Three patients are under treatment, 1 by drilling and 2 by bone grafts.

8. The presence of nonunion is not in itself an indication for operation. The main criterion for operation is nonunion associated with persistence of clinical symptoms and disability and with the patient unable to perform his regular duties.

9. In selection of patients for operation, an attempt should be made to rule out those showing psychoneurotic traits or harboring a desire to avoid going back to duty. Unless this is done, the best operative results may prove unavailing and not alleviate the patient's complaints.

PENICILLIN OINTMENT—IMPREGNATED GAUZE IN THE LOCAL TREATMENT OF INFECTIONS

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LOCAL administration of penicillin, either alone or in combination with general administration, is often advantageous in the treatment of localized infections in accessible sites. However, the commonly used means of topical application have certain disadvantages. For example, sprinkling of penicillin powder on infected surfaces does not carry the material into crevices and tracts, and as Bodenham [1] has pointed out, the drug may be too rapidly absorbed and excreted by the body; moreover, powdered sodium penicillin in undiluted form is somewhat irritating to the tissues. The instillation of penicillin solutions, though satisfactory in situations in which the instilled material is well retained, is often inefficient because the solution drains away from all but the more dependent portions of the lesion. Gauze packs soaked in penicillin solution require relatively large amounts of the drug, and there are often technical difficulties in maintaining contact with all parts of the lesion and in keeping the dressings properly moistened. Penicillin ointments and creams, as described by Florey and Florey,[2] Clark and coworkers,[3] Bodenham [1] and Taylor and Hughes,[4] are often valuable preparations, but as ordinarily used they may not attain and maintain adequate contact with infected surfaces.

In order to obviate these disadvantageous features of current means of local penicillin therapy, penicillin ointment–impregnated gauze was devised. This material is convenient, effective and economical to use. Its preparation, its characteristics and some of its clinical applications are described herewith.

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PREPARATION OF PENICILLIN OINTMENT-IMPREGNATED GAUZE

The preparation of penicillin ointment–impregnated gauze involves, first, the preparation of the ointment and, second, the impregnation of sterilized gauze strips with the ointment.

Penicillin Ointments.—A number of ointment bases, both alone and in combination, were tested to determine the facility with which they liberate penicillin and also to determine the rate of inactivation of the contained drug. This search for a suitable ointment was instituted because of the paucity of data concerning the activity and the stability of penicillin ointments and because some of the more commonly used preparations were unstable, lasting only ten to fourteen days at 4 C.[4]

In vitro tests for the antibacterial activity of ointments were carried out by means of the cup plate method. Cups, 15 mm. in diameter, were punched in agar seeded with Staphylococcus aureus. In these cups

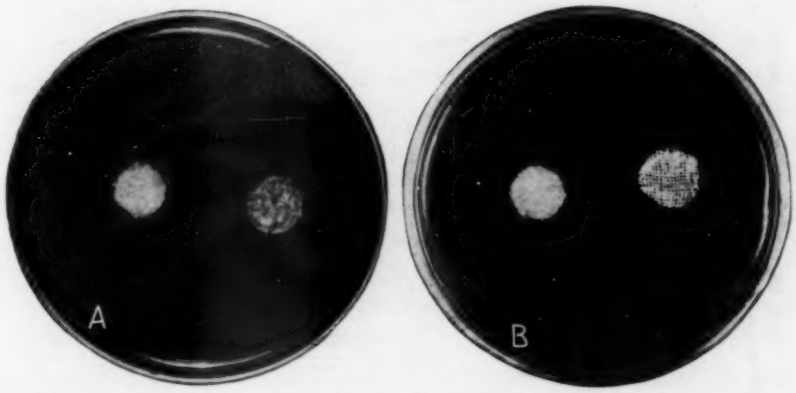

Fig. 1.—Agar plates seeded with Staph. aureus and treated with penicillin preparations. *A*, penicillin ointments after five months at 4 C.: left, penicillin in Aquaphor, showing complete loss of antibacterial activity; right, penicillin in Aquaphor, but with 1 part of Carbowax 1500 to 8 parts of Aquaphor. *B*, left, penicillin ointment (Aquaphor-Carbowax base, 5:1 ratio) filling cup punched out of the agar; right, penicillin gauze impregnated with the same ointment placed on the surface of the agar.

were placed the ointments to be tested, and after incubation at 37 C. for twenty-four hours the distance from the edge of the cup to the farthest limits of inhibition was measured (fig. 1 *A*).

Ointments made up in bases such as hydrous wool fat, Aquaphor, Hydrosorb, Qualatum, Carbowaxes of various molecular weights and combinations of Aquaphor and Carbowax[5] were tested for antibacterial

5. Aquaphor, Hydrosorb and Qualatum are oil in water emulsion type bases manufactered by the Duke Laboratories, Inc., Abbott Laboratories and Almay, Inc., respectively. Carbowaxes are water-soluble waxlike, solid polyethylene

(Footnote continued on next page)

potency. A sodium penicillin solution containing 5,000 Oxford units per cubic centimeter was incorporated into these bases in a ratio of 1 part of the solution to 9 parts by weight of the base, making a potency of 500 units per gram of ointment.

While all the ointments tested gave good inhibition of the organisms, it was evident that those composed of or containing Carbowax gave greater zones of inhibition than the others. Thus, the average zone of inhibition produced by freshly made hydrous wool fat, Aquaphor and Hydrosorb ointments was 11.9 mm., while the average of the ointments containing Carbowax was 18.8 mm. (fig. 2). Moreover, the activity of the penicillin was lost more slowly in ointments containing Carbowax (fig. 1 *A*). After seventy days, the average loss of activity in Aquaphor, the most effective ointment not containing Carbowax, was 26.5 per cent

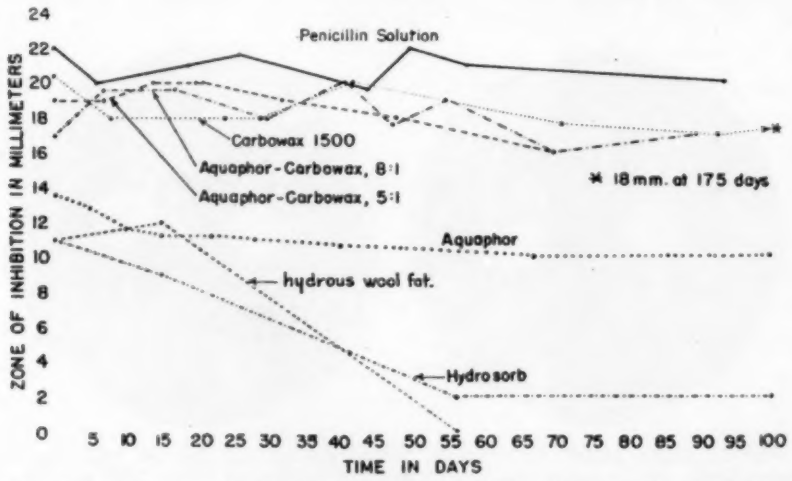
ZONE OF INHIBITION IN MILLIMETERS
TIME IN DAYS
Penicillin Solution
Carbowax 1500
Aquaphor-Carbowax, 8:1
Aquaphor-Carbowax, 5:1
* 18 mm. at 175 days
Aquaphor
hydrous wool fat.
Hydrosorb
0 2 4 6 8 10 12 14 16 18 20 22 24
5 10 15 20 25 30 35 40 45 50 55 60 65 70 75 80 85 90 95 100

Fig. 2.—Curves showing the ability of six penicillin ointments to inhibit Staph. aureus after periods of storage in the refrigerator. The ointments containing Carbowax gave greater inhibition and lost their potency more slowly than those not containing Carbowax; in fact, they lost their potency only a little more rapidly than did the control solution of penicillin. The ointments all contained 500 units of penicillin per gram; the penicillin solution contained 5,000 units per cubic centimeter, and 1 drop was used.

as compared with the average loss of 11.7 per cent for the three ointments containing Carbowax (fig. 2). The rate of inactivation of the Carbowax-containing ointments was not appreciably greater than that of a penicillin solution containing 5,000 units per cubic centimeter of isotonic

glycols manufactured by the Carbide and Carbon Chemicals Corp.; they consist of mixtures of polyethylene glycols of varying molecular weights. Thus, Carbowax 1540 consists of a number of compounds with an average molecular weight of 1540. Carbowax 1500 is a 50:50 mixture of Carbowaxes 1540 and 300.

solution of sodium chloride, which lost 6 per cent of its activity in seventy days (fig. 2).

The reason for devising mixtures of Aquaphor and Carbowax was that the ointments composed of Carbowax alone did not have the desired physical characteristics over the range of temperatures at which the ointments were used. Thus Carbowax 1500 and 1540 when containing penicillin solution were liquid at body temperature (98.6 F. [37 C.]). When Carbowaxes of higher molecular weight were added to correct this defect, the refrigerated ointment became too hard for easy spreading. Since the Aquaphor-Carbowax mixtures retain the advantages of effective liberation of penicillin and long retention of penicillin activity exhibited by the Carbowax ointments and yet retain their ointment characteristics, they have been adopted for use not only as ointments but also in the preparation of penicillin gauze. The optimum Aquaphor : Carbowax ratio was found to be 5 to 1.

A satisfactory ointment containing 500 Oxford units of penicillin per gram is prepared according to the following formula: 150 Gm. of Aquaphor, 30 Gm. of Carbowax 1500 and 100,000 units of sodium penicillin dissolved in 20 cc. of isotonic solution of sodium chloride. The Aquaphor-Carbowax mixture is sterilized by autoclaving and is cooled to 65 C., at which temperature the penicillin solution is added with vigorous stirring until solidified or until poured on gauze strips. As penicillin becomes more plentiful, it may be advisable to increase the potency of the ointment to 1,000 units per gram. The ointment is stored in the refrigerator, where the loss of activity is less than one fourth as rapid as at room temperature.

Penicillin Gauze.—Penicillin gauze is prepared by pouring the melted penicillin ointment described on sterile gauze strips cut from 2 inch (5 cm.) roller gauze bandages into lengths of about 7 inches (18 cm.). The ointment, melted by heating to not over 65 C. is evenly distributed through the gauze, and the material is allowed to stand in the warm room (37 C.) for an hour to complete the even impregnation of the gauze. Thereafter the penicillin gauze is stored in the refrigerator, where it retains its activity for six months or more.

Two hundred grams of ointment being used for each one hundred and fifty strips, the gauze is thoroughly impregnated and yet the meshes are left open. It may be calculated that since the ointment contains 500 units of penicillin per gram each strip contains 665 units, while each square centimeter of gauze contains approximately 7.4 units.

CHARACTERISTICS OF PENICILLIN GAUZE

A single layer of penicillin gauze, 1 cm. in diameter, placed on the surface of an agar plate seeded with Staph. aureus gave an average zone

of inhibition of 12 mm. from the edge of the gauze after twenty-four hours' incubation in a series of sixteen tests. A 15 mm. disk of penicillin gauze gave almost as much inhibition as a 15 mm. cup of ointment (fig.1 *B*). Obviously, penicillin ointment–impregnated gauze effectively liberates the penicillin under these conditions.

An increase in the number of layers of gauze applied to an agar test plate gave slightly increased zones of inhibition. In one test using penicillin gauze made with penicillin in Aquaphor ointment, the inhibition was as follows: one layer, 8 mm.; two layers, 11 mm., and three layers, 13 mm. In a test using gauze impregnated with a penicillin ointment with a Carbowax-Aquaphor base, the inhibition was as follows: one layer, 16 mm.; two layers, 16.5 mm., and three layers, 16.5 mm.

How long does the penicillin persist in the penicillin gauze when applied to an infected lesion? To answer this query, pieces of gauze 1 cm. in diameter were cut from strips which had remained in the lesions of patients for twenty-four and forty-eight hours, and these were tested on agar plates inoculated with Staph. aureus. Similar disks of unused penicillin gauze were simultaneously tested for controls. In fourteen such tests the average zone of inhibition exhibited by the gauze used for twenty-four hours was 50.4 per cent of that of the unused gauze. Thus, if a penicillin gauze strip containing 665 units is used in a wound, about half, or 335 units, is steadily fed into the infected surface over the twenty-four hour period. That the penicillin is largely fed into the wound instead of being inactivated by the body heat is indicated by the finding that penicillin gauze when hung up in an incubator at 37 C. for twenty-four hours loses only 14 per cent of its activity.

The rate of penicillin loss is much more rapid when there is profuse drainage through the gauze. Thus, in 2 patients, 1 having a salivary fistula and the other epiphora from an exposed eyeball, the saliva and tears respectively carried away all the penicillin so that the penicillin content of the gauze was reduced to zero after twenty-four hours. The presence of penicillin-resistant organisms may also accelerate the loss of potency. The presence of fever was not observed to increase materially the rate of inactivation of penicillin gauze.

Two assays of penicillin gauze after a forty-eight hour sojourn in infected lesions revealed no activity in one and the persistence of 31 per cent of the original activity in the other. These results suggest the advisability of daily dressings for maximum therapeutic effect.

Pus removed from an abscess into which penicillin gauze had been inserted twenty-four hours previously was tested by the agar cup plate method. A zone of inhibition of 9 mm. was observed; this was about the same degree of inhibition as that produced by a solution containing 5 units of penicillin per cubic centimeter. Pus from another abscess, in

which there was a moderate number of penicillin-resistant staphylococci, gave only 2.5 mm. inhibition after a twenty-four hour period. Pus from a similar lesion but after a forty-eight hour interval after the insertion of the gauze gave no inhibition.

TECHNIC FOR CLINICAL USE OF PENICILLIN GAUZE

It cannot be too strongly emphasized that penicillin gauze is not intended to replace established surgical procedures such as those required for the establishment of free drainage and for the removal of devitalized tissue. However, the effective local therapy attained with penicillin gauze may often make it feasible to use more conservative measures than usual.

Technic of Application.—For infected flat surfaces, penicillin gauze is simply laid on the lesion and covered with a sterile cotton or gauze dressing. If the surface is irregular, care is exercised to press the gauze into each crevice and then to pack cotton into these depressions before the final dressings are applied. A single layer of penicillin gauze is ordinarily used because if there is any drainage it is desirable to allow it to pass through the meshes of the gauze so that the medicine is not pushed away from the treated surface by collections of exudate. If, however, there is little drainage and maximum penetration is desired, two or three layers of gauze may be applied.

For infected tracts, penicillin gauze may be inserted as a wick. When the discharge is copious and the opening is not wide, it may be desirable to use a slender wick so that the drainage is not blocked. If the discharge is moderate, the tract or cavity may be packed tightly with the gauze.

Ordinarily, the penicillin gauze dressings are changed daily because, as previously mentioned, the penicillin content is largely used up in forty-eight hours. When the infection is not severe, however, less frequent dressings are satisfactory. Other circumstances may also require less frequent dressings, as, for example, over skin grafts which might be pulled off by disturbance of the dressing too early.

Inasmuch as there are a number of organisms which are insensitive to penicillin, it is imperative that an aseptic technic be used. The chances of more bacteria being carried into the lesion are reduced by application of an antiseptic to the surrounding skin.

Tests for Sensitivity of Organisms to Penicillin.—It is desirable to determine as soon as possible whether or not the organisms producing a given infection are sensitive to penicillin. This may be done by any of a number of sensitivity tests, but the radial streak method, described

elsewhere,[6] has the advantage of being simple and convenient as well as being accurately quantitative. With this test one may test material from several lesions simultaneously by streaking it radialwise on a blood agar plate and then placing a disk of penicillin gauze in the center. The sensitivity of the organisms to penicillin may be determined after as short a period of incubation as eight hours. The degree of sensitivity is expressed in per cent, the inhibition of Staph. aureus, strain 209-P,[7] being taken as 100 per cent (fig. 3). Infections caused by organisms with a sensitivity reading of 50 to 150 per cent usually respond dramatically to local therapy with penicillin ointment–impregnated gauze. When the organisms show a sensitivity of 10 to 50 per cent, the response

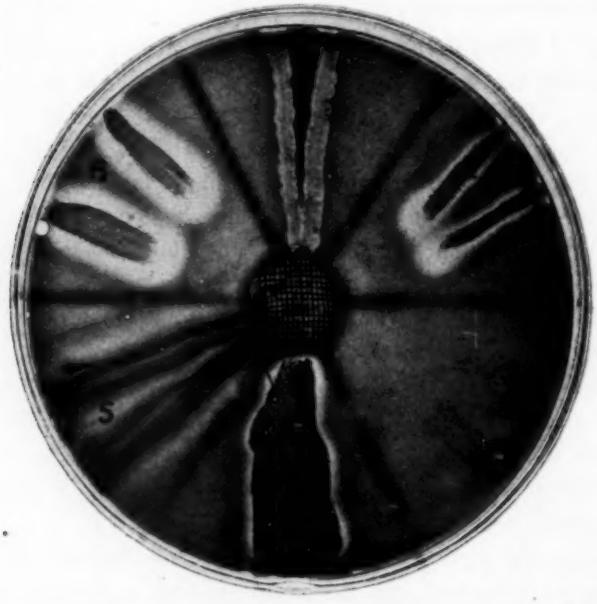

Fig. 3.—"Radial streak" test to determine the sensitivity to penicillin of organisms from infected lesions. Sector *1*, Bacillus coli from a furuncle which did not respond to penicillin gauze. Sensitivity, zero. Sector *2*, Staph. aureus from furuncle cured by penicillin gauze (case 1). Sensitivity, 106 per cent. Sector *3*, Staph. aureus from a carbuncle cured by intramuscular penicillin plus penicillin gauze (case 2). Sensitivity, 131 per cent. Sector *4*, Staph. aureus from facial folliculitis not cured by penicillin gauze. Sensitivity, 6 per cent. Sector *5*, Staph. aureus from post-chemosurgical wound after removal of an old burn ulcer. Infection not cured by penicillin gauze. Sensitivity, zero. Sector *6*, control Staph. aureus, strain 209-P. Sensitivity, arbitrarily taken as 100 per cent. The light zone around some of the streaks represents hemolysis.

6. Mohs, F. E.: A Simple Quantitative Test for the Penicillin Sensitivity of Bacteria: The "Radial Streak" Method, J. Lab. & Clin. Med. **30**:800 (Sept.) 1945.

7. A culture of Staph. aureus 209-P was obtained from the Food and Drug Administration through Dr. Albert C. Hunter.

is apt to be less dramatic but, nevertheless, favorable. A sensitivity below 10 per cent usually means that the clinical response will be sluggish or absent and that other means of therapy are indicated.

THERAPEUTIC RESULTS IN INFECTIONS TREATED WITH PENICILLIN GAUZE

A total of one hundred and four lesions were treated locally by means of penicillin ointment–impregnated gauze. In this group there was no instance of allergic or other untoward reaction to the medicine.

Furuncles.—Eleven furuncles in the pointing stage were conservatively incised, the pus gently removed and the cavity packed with penicillin gauze. All were sterilized within a few days (often by forty-eight hours) with one exception, a large boil over the lumbar portion of the spine caused by Bacillus coli, which was completely resistant to penicillin (fig. 3, sector 1). Associated with the rapid sterilization of these lesions was a correspondingly rapid clinical improvement. In patients who had previously had similar lesions there was noted a more rapid recovery with penicillin gauze therapy than with treatments previously used; the case of a patient illustrating this point follows.

CASE 1.—In the patient, F. H. B., aged 54, during the course of one week a greatly inflamed and painful furuncle, 2 cm. in diameter, developed on the dorsum of the hand. It had just pointed and was beginning to discharge grayish pus. The opening was sufficient to allow the removal of some of the pus and the insertion of a strip of penicillin gauze measuring 5 by 30 mm. A single layer of penicillin gauze 2 cm. in diameter was applied to the surface of the skin and a gauze dressing applied. Smears and cultures revealed Staph. aureus, and the radial streak test showed the penicillin sensitivity to be 106 per cent (fig. 3, sector 2).

By twenty-four hours there was less inflammatory reaction, but smears showed an occasional organism and the cultures showed staphylococci. By forty-eight hours, however, no organisms were found by smear or culture. Clinically, all the soreness and most of the inflammation had disappeared. Cultures taken four days later were also negative. When last seen, nine days after the first visit, the lesion was healed.

This patient had previously had furuncles of similar nature, which had taken one week to develop, one week to drain and one week to heal. It is estimated that the rapid sterilization produced by the local penicillin gauze therapy shortened the duration of the process by at least five days.

Carbuncles.—A large carbuncle on the back of the neck was treated. It responded well to local penicillin gauze therapy, though it had not responded satisfactorily to either sulfadiazine or intramuscular therapy with penicillin.

CASE 2.—In the patient, S. E. W., aged 67, several "bunches" on the back of the neck developed sixteen days before the institution of penicillin gauze therapy. Four days after the onset one of the masses had broken open, discharging much pus, and during the next few days several more openings developed. The patient's

condition became worse despite hot wet packs and sulfadiazine, 1 Gm. every four hours for five days. On admission to another service, his temperature was 100 F. The tender inflamed mass, which involved the entire back of the neck, continued to drain large amounts of pus for the next five days, during which allantoin and urea packs were applied and penicillin was given intramuscularly in doses of 15,000 units every three hours. The temperature was reduced but did not stay normal.

When local penicillin gauze therapy was instituted, the mass measured 10 by 11 cm. and there were six tracts, which were from 24 to 62 mm. deep (fig. 4 *A*). About 150 cc. of pus was expressed. Smears and cultures revealed numerous organisms identified as Staph. aureus. The organisms were highly sensitive to penicillin, giving a reading of 131 per cent by the radial streak test (fig. 3, sector 3).

Penicillin gauze wicks measuring 2.5 by 8.5 cm. were inserted into the bottom of each tract with the use of a blunt probe. The intramuscular administration of penicillin was continued. By the next day the swelling had reduced to 8 by 8.5 cm. The amount of discharge became less each day, the temperature remained

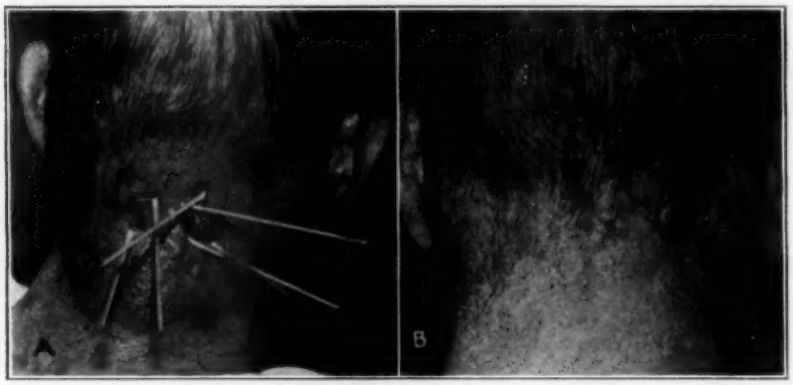

Fig. 4.—*A*, carbuncle with applicators inserted in six sinuses, the depths of which varied from 24 to 62 mm. *B*, after cure by intramuscular administration of penicillin plus insertion of penicillin gauze strips, showing minimal scar.

normal and the symptoms subsided; so after three days the intramuscular administration of penicillin was stopped and the patient was discharged from the hospital.

He returned daily for insertion of penicillin gauze. There was about 25 cc. of pus each day, and cultures revealed staphylococci until the seventh day, when cultures became negative. As the tracts filled in from the bottom, the strips were shortened accordingly. Strips of penicillin gauze were placed on the skin over the central part of the carbuncle, and no new pustules developed there. However, a pustule, 5 mm. in diameter, developed in the left postauricular region, and this responded rapidly to incision and the insertion of penicillin gauze. Further recurrences were obviated by the placing of penicillin gauze over the surrounding skin to eliminate the pathogens. In one month the lesion had healed. The final scar was minimal (fig. 4 *B*).

Other Surface Infections.—Thirty-one other surface infections were treated by the application of penicillin ointment–impregnated gauze. The results were as follows: four infected diabetic ulcers, cured; three

stasic ulcers, two cured and one improved; three cases of paronychia; cured; two areas of cellulitis around navel in infants, cured; three areas of cellulitis elsewhere, cured; three areas of infective eczematoid dermatitis, cured; one chronic indolent ulcer on neck, cured; three infected burn ulcers, cured or much improved; one infected corn, improved temporarily, but lymphangitis developed, which responded to oral administration of sulfadiazine; three areas of impetigo, cured in two to four days; two infected sebaceous cysts, infection subsided, and three areas of pustular folliculitis, two cured and one not improved. The last infection was the only one in this group of predominantly staphylococcic infections which did not show some degree of favorable response; it was caused by a strain of Staph. aureus with a sensitivity of only 6 per cent, as determined by the penicillin sensitivity test (fig. 3, sector 4).

Postoperative Wounds.—Penicillin gauze may be used in postoperative wounds either for the prevention of infection or for the treatment of established infections. In the chemosurgery clinic, thirty-one wounds following chemosurgical excision of cancers [8] from locations where the avoidance of contamination was difficult were dressed with penicillin gauze. All but two responded satisfactorily. One was a lesion infected with a strain of Staph. aureus with a sensitivity of zero as determined by the radial streak test; this infection responded promptly to scarlet red gauze,[9] and healing then proceeded uneventfully. The other exception was a temporal wound with a large area of exposed temporal bone; while the Staph. aureus producing the infection was originally fairly sensitive to penicillin (36 per cent), the presence of the dead bone prevented rapid sterilization and the organisms became less sensitive (19 per cent), with consequent worsening of the infection. Switching to streptomycin ointment-impregnated gauze, to which the organisms were more strongly sensitive (73 per cent), resulted in prompt and complete sterilization of the wound.

After the amputation of gangrenous parts by chemosurgical treatment,[10] penicillin gauze was found effective in avoiding infections in patients whose resistance was lowered by diabetes and arteriosclerosis. In 11 patients healing was uncomplicated by infection, even though in 2 healing was slow due to severe circulatory impairment. The complete lack of any irritating effect on the tissues by the penicillin gauze was especially advantageous in this group.

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8. Mohs, F. E.: Chemosurgery: A Microscopically Controlled Method of Cancer Excision, Arch. Surg. **42**:279 (Feb.) 1941.

9. Bettman, A. G.: A Simpler Technic for Promoting Epithelization and Protecting Skin Grafts, J. A. M. A. **97**:1879 (Dec. 19) 1931.

10. Mohs, F. E.; Severinghaus, E. L., and Schmidt, E. R.: Conservative Amputation of Gangrenous Parts by Chemosurgery, Ann. Surg. **114**:274 (Aug.) 1941.

Seventeen other postchemosurgical wounds following the removal of two radiation ulcers, three plantar warts, two infected pilonidal cysts, one blastomycotic lesion, four nevi, one keratosis, one chronic infection, one hemangioma and two infected burn ulcers; all healed uneventfully with the exception of one of the burn ulcers, which became infected with a strain of Staph. aureus having complete resistance to penicillin, as indicated by the radial streak test (fig. 3, sector 5).

On other services in this hospital penicillin gauze has been effective in the treatment of a number of infected incisions, stitch abscesses, postmastoidectomy infections, infected tooth sockets and infected grafts. However, since bacteriologic studies are lacking for most of these cases, they are just mentioned here to give some suggestion of the variety of uses for penicillin gauze.

Osteomyelitis.—Osteomyelitis in 2 cases was definitely improved but not completely sterilized by the use of penicillin gauze. In both cases the penicillin eradicated the chief pathogens, but the presence of dead bone allowed the persistence of a few penicillin-resistant organisms. Removal of the sequestrum appears to be essential for a complete cure.

COMMENT

The effectiveness of penicillin ointment–impregnated gauze in the local therapy of infections is probably due largely to the steady transfer of penicillin from the gauze to the infected tissues throughout the twenty-four hour period between dressings. As shown by the assays of penicillin gauze removed from wounds, about one half of the contained penicillin is transferred to the tissues during a twenty-four hour period. Since each square centimeter of penicillin gauze originally contains 7.4 units of penicillin, there is a transfer of about 3.7 units to each square centimeter in twenty-four hours.

That the penicillin is transferred to exudates is clearly indicated by the assays of pus from abscesses treated with penicillin gauze. Some of these tests showed levels well above the blood levels after parenterally administered penicillin. This capacity of penicillin gauze to maintain high local levels of penicillin over prolonged periods probably accounts for its ability to sterilize infections which are resistant to intramuscular administration of penicillin alone, as, for example, the carbuncle described in case 2. When there is some evidence of spread of infection from the local site, it is, of course, advisable to administer antibiotic substances by the systemic as well as by the local route. The dictum, enunciated by Meleney,[11] that local penicillin therapy ordinarily is

11. Meleney, F. L.: Medical Progress: Some Practical Points in the Administration of Penicillin in the Treatment of Surgical Infections, New York Med. (no. 11) **1**:15 (June 5) 1945.

sufficient in patients with temperatures below 101 F. but that systemic administration is required when the temperature is higher appears to be valid.

Although penicillin definitely is the most effective drug against infections caused by organisms which are sensitive to it, there is the unfortunate circumstance that some organisms are partially or completely insensitive to it. Luckily, most of the more strongly pathogenic microbes are sensitive to penicillin, and when these are removed from a lesion harboring a mixed infection there is often distinct clinical improvement.

Not infrequently, however, troublesome penicillin-resistant infections are encountered. For these it would be ideal to have on hand a variety of antibacterial agents impregnated in gauze, with tests to determine which is most effective for a given infection. A start in this direction has been made by the use of streptomycin ointment–impregnated gauze; this antibiotic drug is effective not only in lesions caused by most of the penicillin-resistant gram-negative bacilli but also against infections caused by penicillin-resistant strains of ordinarily penicillin-sensitive organisms, such as Staph. aureus.

The impregnation of gauze with ointments is not new. Petrolatum and boric acid ointment gauze have been used for years. Scarlet red gauze as developed by Bettman [9] has valuable antibacterial as well as epithelial stimulating activity. Ointment–impregnated gauze has several advantages over gauze on which ointment is spread. First, the former has open meshes through which exudates may freely pass so the medicine is not pushed away from the infected surface. Second, ointment–impregnated gauze lends itself better to close apposition to irregularly contoured lesions and to insertion into infected tracts and sinuses. Third, the reduced tendency for exudates to collect under ointment–impregnated gauze reduces the incidence of infective eczematoid dermatitis, which results from exudates contacting the skin around infected lesions.

SUMMARY AND CONCLUSIONS

The preparation of effective and stable penicillin ointments is described. The preparation, characteristics and clinical use of penicillin ointment–impregnated gauze are considered, and the results of local penicillin therapy with this agent in a series of 104 cases are reported.

The local therapy of infections by penicillin gauze facilitates the maintenance of effective levels of penicillin in wounds with a single application a day, with resultant savings in time and material. The accuracy with which penicillin gauze can be applied to and kept in constant contact with infected surfaces makes possible a steady transfer of the penicillin from the gauze to the infected tissues over prolonged periods.

ADDENDUM

The addition of various antibacterial agents to penicillin ointments for the purpose of eliminating the penicillin-resistant organisms in mixed infections has been found advantageous. Parachlorophenol in 1:400 concentration, as suggested by Meleney,[12] is as effective as any agent tried so far. It is added to the Aquaphor-Carbowax mixture at the same time as the penicillin solution. The penicillin gauze with the added parachlorophenol may be used in the radial streak sensitivity test, but if the sensitivity to penicillin itself is being tested for it is, of course, necessary to omit any additional antibacterial agents.

Prof. Paul F. Clark and Prof. Erwin R. Schmidt gave helpful advice, and Mrs. Eleanore Sweitzer gave technical assistance.

12. Meleney, F. L.; Johnson, B. A.; Pulaski, E. J., and Colonna, F.: Treatment of Mixed Infections with Penicillin, J.A.M.A. **130**:121 (Jan. 19) 1946.

A SURGICAL SPECIMEN CONSISTING OF A PARTIALLY DEVELOPED PARASITIC FETUS

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A MAN, in search of immediate medical attention, came to me as he wanted some doctor, the nearest doctor, to attend his deformed offspring, a son, who was suffering from bronchopneumonia.

CLINICAL PICTURE

On examination of the child I discovered an amazing monstrosity—indeed the only one of its kind I have ever encountered—which had been under exhibition at a circus in a nearby town.

He was a normal boy who had attached to his epigastrium a half-body (fig. 1) consisting of a normal-shaped abdomen with an atrophied

Fig. 1.—A close-up of the epigastropagus.

arm at the upper part and well developed thighs, legs, feet and genital organs at the lower part.

As interesting details, I must mention that this monstrosity was able to urinate, did not have an anus (fig. 2), presented only passive movements of adduction and abduction in his hip joints and had only four toes on each foot. Yet the development of this parasitic monstrosity was similar to that of the homologous parts of the boy (fig. 3). During examination, the child showed no pain when the skin of the monster was pinched. There was no mobility or noise in the monstrosity which

From the Colegio Mexicano Medicina y Cirugía.

might indicate the existence of heart and lungs and no reaction to galvanic current. Furthermore, there were no active movements.

The patient, J. I. L., was born in the state of Sinaloa, Mexico, on Dec. 28, 1944; his age at operation was 2 months and 23 days. During

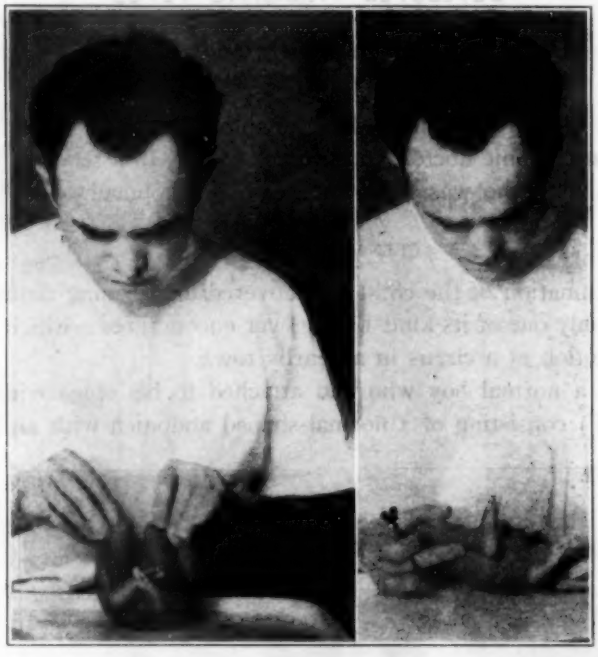

Fig. 2.—Passive movements of the monster.

Fig. 3.—Rear view of the monstrosity. Note absence of anus.

pregnancy his mother had shown an intense positive reaction to the Wassermann test. There is no relationship between the parents. The pregnancy had been normal except for the fact that the mother allegedly felt many movements; birth occurred at the normal period.

Breast feedings were alternated with feedings of condensed milk. The laboratory examinations disclosed identical compositions for the two urines.

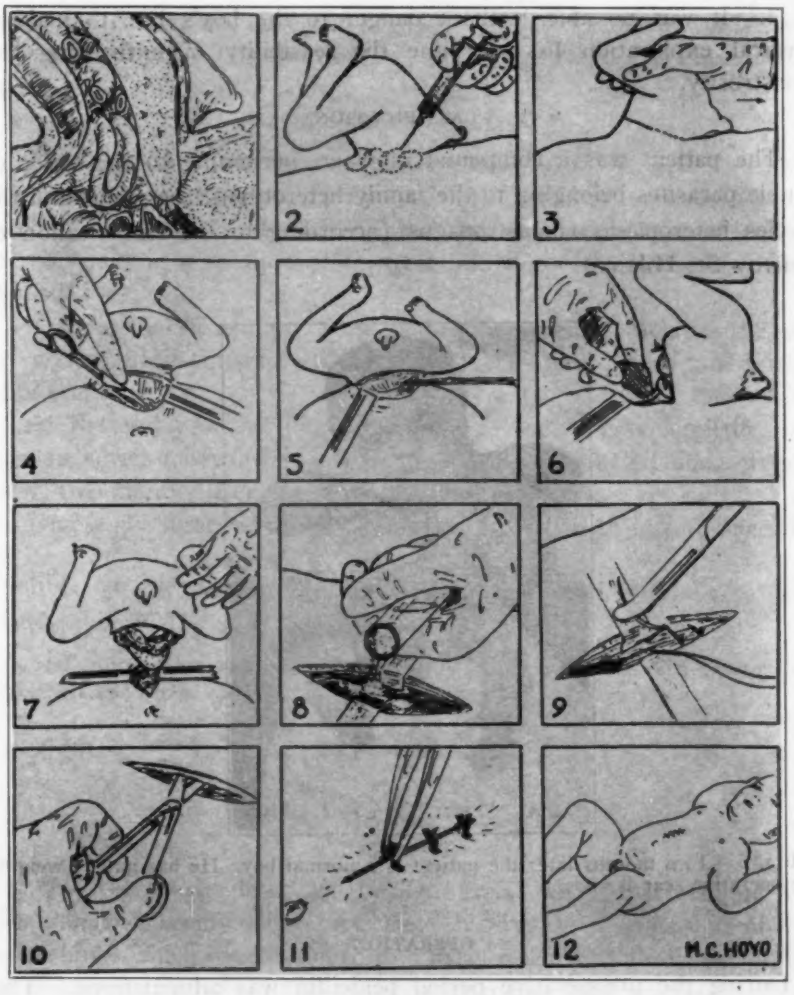

Fig. 4.—Drawings of the operation.

After treating the child for bronchopneumonia, I suggested an operation basing my suggestion on the following considerations:

1. It being established that the child's heart was subject to extreme exertion in pumping blood to both bodies, his life could not be guaranteed.

2. When I compressed the junction of the two bodies there were no untoward reactions, and it convinced me that the organs of the monstrosity were unimportant.

3. From the standpoint of esthetics, such a grotesque creature was doomed to misery.

4. It was possible, without danger to the boy's life, to make a surgical exploration to determine the feasibility of extirpating the monstrosity.

CLASSIFICATION

The patient was a compound monster, pertaining to the order of double parasites belonging to the family heterotypus, the genus and the species heteropagus epigastropagus (according to the classification of Geffroy St. Hilaire).

Fig. 5.—Two months later the patient is a normal boy. He has gained weight. The operative scar is shown.

OPERATION

During the preoperative period penicillin was administered. The operation (see fig. 4) was performed with the patient under local anesthesia. A circular incision (about 5½ inches [14 cm.] in circumference) was made at the union of the bodies, including skin and fascia. The bladder of the monster was subjected to a blunt dissection and ligated in its upper pole.

After the intestines of the monstrosity—inflamed and containing yellow pus—were found tightly adherent to those of the child, with

some difficulty it was possible to separate them. An analysis disclosed no germs in the pus. Finally, an atrophied liver was found joined to the normal liver of the child, it also being possible in the end to separate it. A semi-important artery and vein were ligated at the upper part of the fascia. After 2.5 Gm. of sulfathiazole had been placed inside the cavity, the different structures of the abdomen were sewed with surgical gut. The child's efforts prevented the use of clips for the skin.

POSTOPERATIVE COURSE

The temperature after the operation was 38 to 39.5 C. (100.4 to 103.1 F.) for the first two days; it was 41 C. (105.8 F.) at forty-eight hours, receding after a bath. Penicillin (30,000 units) was administered daily for two days in a solution of dextrose and isotonic solution of sodium chloride.

A superficial disruption of the wound forced me to mobilize the skin by undercutting and to sew it again, but there were no further complications.

At the end of eight days, the child presented good appetite, had regular bowel movements, urinated normally and had gained weight. Now, two months later (fig. 5) he is a normal boy.

I have not dissected the monstrosity, as I wish to have a specialist do it.

It is not my desire to generalize, inasmuch as this is a case completely abnormal.

Dr. Ramirez Ruiz helped as first assistant in the operation, and Nurse Rosa Maria Mercado took care of the baby before and after the operation.

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THE specimen described by Dr. Luis Pavón Sarrelangue was received in my laboratory Dec. 22, 1945. It consisted of two lower limbs which were attached to a mass resembling the lower part of an abdomen (fig., *A*). The upper portion had been severed from the abdomen of the child to whom it was attached. This operation took place two months and twenty-three days after birth.

Roentgen examination revealed well developed bones in the lower extremities (fig., *B*). Each extremity presented a femur, tibia, fibula,

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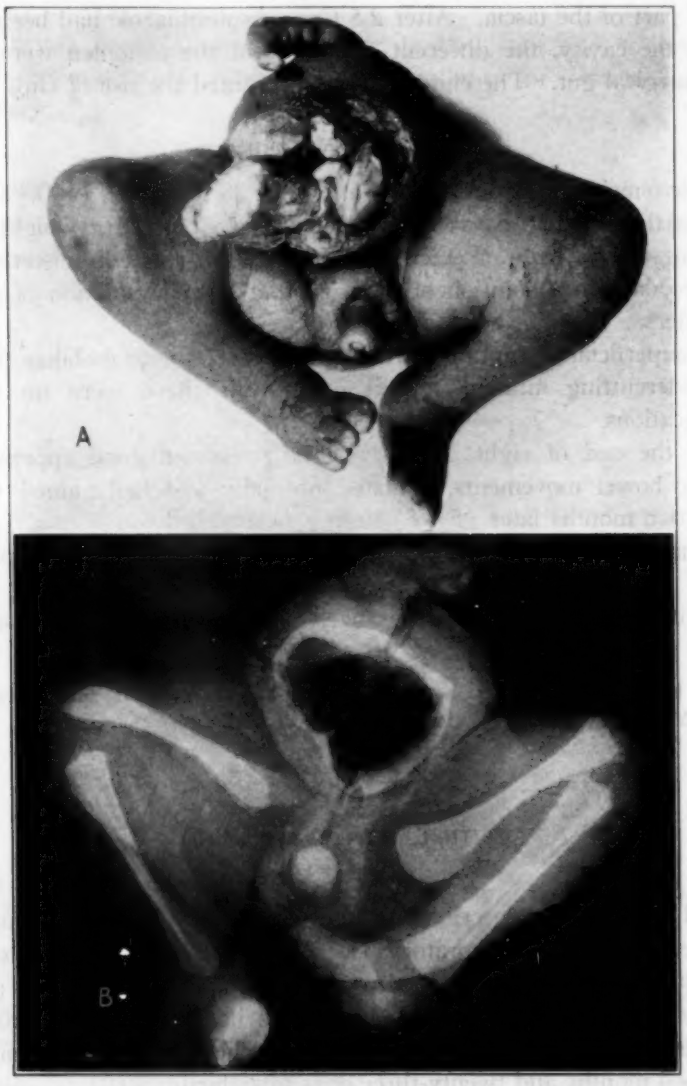
several tarsal bones, four metatarsal bones and three phalanges attached to each metatarsal bone. Three bones were present in the pelvis. Two appeared to be descending pubic rami, and the other, which is a flat oval



A, parasitic monster consisting of two lower limbs, genital organs, abdomen and rudimentary arm; *B*, roentgenogram of monster, showing well developed bones in lower extremities.

bone with an inferior cleft, probably represented the fused wings to the iliac bones. No evidence of a spinal column could be made out. In the terminal portion of an appendage attached to the most superior

part of the specimen were three phalangeal bones, which represent an abortive attempt to form a finger.

The specimen was covered by brown, well preserved, normal skin except over the area by which it had been attached to the twin. This cut surface was directed anteriorly and permitted a view into the abdominal cavity. Attached to the most superior portion of the posterior surface was a single appendage, which tapered toward the distal end and exhibited a well formed finger nail. It measured 5 cm. in length.

On the anterior surface immediately below the line of incision were a large well formed penis and scrotum. The penis was 2 cm. long, was normally developed and contained a normal urethra. No testes could be demonstrated.

The skin over the back presented a smooth surface, which extended without a break to the base of the scrotum; no anus had been formed.

The thighs measured 11 cm. in length, the legs 11 cm. and the feet 7 cm. A pronounced contracture of each knee due to shortening of the skin over the posterior surface prevented extension of this joint. From the anterior surface of the knee to the popliteal space was 6 cm. Each foot had a well developed heel, metatarsal region and four normal toes.

The body cavity was partially divided into two sections by a transverse fold, which extended from above downward and separated the left one third from the right two thirds. Several loops of intestine, showing extreme variation in caliber and measuring about 15 cm. in total length, occupied the anterior part of both body cavities. Both ends were rounded, and neither had an opening.

Behind the loops of intestine lying against the posterior wall of the body cavity and immediately in front of the iliac bone was a well formed kidney of the approximate size normally found in a newborn infant. From the medially directed renal pelvis, a ureter descended, which emptied into the lower portion of a large, thick-walled urinary bladder. The bladder measured approximately 4 cm. in total length, and the wall was 4 mm. thick. Leading from the inferior portion and extending through the penis was a normal urethra. Surrounding the proximal portion of the urethra and extending upward behind the bladder were two closely associated masses, which proved on histologic examination to be prostate gland and seminal vesicles.

Histologic examination was fairly satisfactory, and only mild postmortem degeneration was evident. The intestine was composed of normal muscle layers; the mucosa had been desquamated. The bladder wall was lined with normal epithelium, which was surrounded by normal muscle. The kidney contained normally arranged tubules and glomeruli. Several sections from the wall of the abdominal cavity contained normal fat, muscle, lymphoid tissue and blood vessels. The clots within the

vessels contained a large number of immature red blood cells. Sections from the uppermost portion of the abdominal cavity showed a diffuse infiltration of inflammatory cells.

The surgeon stated that a small liver belonging to this portion of the infant was found at operation. None was present in the specimen at the time of examination.

SUMMARY

A parasitic fetus consisting of two legs and the lower part of the abdomen which had been surgically removed from its point of attachment to the anterior abdominal wall of an infant 2 months and 23 days old was observed. Each lower limb possessed a femur, tibia, fibula, tarsal bones, four metatarsal bones and three terminal phalanges attached to each tarsal bone; pubic rami and a common iliac bone composed the pelvis. No spine was present. Within the abdominal cavity were intestine, bladder, kidney and ureter. Surrounding the urethra near its connection with the bladder was a prostate gland, and extending upward from it were seminal vesicles.

REVIEW OF UROLOGIC SURGERY

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KIDNEY

Hydronephrosis.—Gibson [1] classified the type of obstruction that causes hydronephrosis at the ureteropelvic junction, evaluated the methods of surgical treatment and emphasized the factors that contribute to the successful outcome of the operation.

Obstructions of the ureteropelvic junction may be divided advantageously into three types or groups: (1) kinking and distortion at the ureteropelvic junction by extrinsic adhesions, fibrous or vascular bands or anomalous vessels; (2) intrinsic obstruction at the ureteropelvic junction by strictures from thickening of the musculature, hyperplastic fibrous tissue and a fibrous contracture producing a small stoma, and (3) another type of intrinsic obstruction from valve formation, caused by high insertion of the ureter into the pelvis. These types of obstruction may coexist. The inner caliber of the ureteropelvic junction cannot be determined accurately by external inspection or palpation. Therefore, if extrinsic obstruction is present, the surgeon should not be content in believing that it is the sole cause of the hydronephrosis until he has opened the pelvis through a small incision and calibrated the ureteropelvic junction. This can be done with the tip of a hemostat or a 12 to 14 F. bougie passed downward through the ureteropelvic junction.

1. Gibson, T. E.: Hydronephrosis: Classification and Plastic Repair of Ureteropelvic Obstructions, Surg., Gynec. & Obst. **80**:485-496 (May) 1945.

Gibson has divided the numerous pyeloplastic procedures into four basic types: (1) reimplantation of the sectioned ureter into the pelvis at its most dependent part (Kuester), with or without excision of the redundant pelvis; (2) longitudinal incision and transverse closure (Fenger); (3) a Y incision with a V closure (Schwyzer and Foley), and (4) lateral anastomosis of pelvis and ureter (the original Trendelenburg operation, of which there are many interesting and useful variations).

Gibson said that ureteral splinting and intubation, with the necessary nephrostomy, pyelostomy or ureterostomy drainage, is the most important single factor that contributes to a successful end result in this highly technical field. He has found that the various types of nephrostomy tubes, with ureteral catheters and splints attached, are unsatisfactory because the splinting portion of the tube which goes down the ureter is not sufficiently rigid and tends to pass backward into the pelvis, where it coils and completely defeats its purpose.

The T tube offers a much more satisfactory type of drainage both for nephrostomy and for ureteral splinting. It can be cut to size and is easily introduced and removed. It can be used just as readily for ureterostomy as for nephrostomy. Splinting and drainage should be maintained for ten days to three weeks or more, depending on the apparent needs in the individual case.

Gibson said that pyeloureteral splinting and intubation with a T tube does away to a large extent with the necessity of elaborate plastic operations and the delicate suturing they entail.

Adequate exposure is essential for any type of pyeloplasty. The twelfth rib is removed to facilitate adequate exposure, which is essential to the proper performance of any type of pyeloplasty.

In the first type of obstruction, the extrinsic, a simple pyeloureterolysis with nephropexy is all that is necessary. However, the lumen of the ureteropelvic junction should be calibrated before the operation is concluded, and ureteral splinting should be employed if there is much peripelvic and periureteric fibrosis, with angulation or distortion of the upper part of the ureter.

In the second type of obstruction, that is, intrinsic obstruction due to fibrosis and stricture at the ureteropelvic junction, a variety of procedures is available. Gibson prefers the Davis-Rammstedt operation. The pelvis is opened between stay sutures. A Mayo hemostat is pushed down through the ureteropelvic junction, and its jaws are spread gradually until the lumen is more than adequate. Simultaneously, a row of parallel vertical incisions is made about the outside and extended down to the mucosa in order to divide the constricting muscle fibers and scar tissue. This step is followed by splinting or intubation to maintain the caliber of the lumen at 12 to 14 F. until

healing is complete. If this is not feasible, other procedures are available, such as the ureteropyeloneostomy of Kuester or Lubash, or the Schwyzer-Foley methods may be used, with success, in type 2 obstruction.

For type 3 obstruction, involving valve formation with high insertion of the ureter in the pelvis, the original Trendelenburg operation is still eminently satisfactory. This may be modified to include excision of a large part of the redundant renal pelvis, as advocated by Priestley. In type 3 obstruction, one may also use the reimplantation methods of Kuester or Lubash or the anterior or posterior plastic operation of Schwyzer and Foley.

Gibson regards adequate splinting and intubation as more important in obtaining a good result than the most painstaking suturing. The end results in several cases of advanced hydronephrosis in solitary kidneys were cited to support Gibson's contention.

Anomalies.—Goyanna and Greene,[2] in considering duplication of the renal pelvis and ureter, stated that the commonest associated pathologic condition is hydronephrosis or hydroureter or both. Duplication is twice as common on the right side as it is on the left side, and hydronephrosis is nearly twice as common in the lower segment. The higher incidence of pyelonephritis, pyonephrosis and atrophic pyelonephritis in the lower segment may be considered a consequence of the faulty drainage of the hydronephrotic kidney. In all cases of ectopic ureter and in all cases in which ureterocele is associated with duplication, the ureter from the upper pelvis was the one affected.

The following roentgenographic signs are suggestive of duplication: (*a*) elongated renal shadow, (*b*) presence of a region of kidney with no means of drainage and (*c*) characteristic shape of the visualized pelvis. Excretory urography alone cannot be depended on to distinguish complete duplication from incomplete duplication of the ureter unless the entrance of both ureters into the bladder is clearly seen. Cystoscopy and retrograde pyelography, although helpful, may fail when the supernumerary orifice is hidden or when the duplication is incomplete. A history of congenital incontinence associated with normal micturition is strongly suggestive of duplication and an ectopic ureter.

Nation[3] reported 34 instances of horseshoe kidney that were disclosed in 15,728 autopsies, an incidence of 1:468 bodies examined. Twenty-seven (79 per cent) of the patients were men, and 7 (21 per

2. Goyanna, R., and Greene, L. F.: The Pathologic and Anomalous Conditions Associated with Duplication of the Renal Pelvis and Ureter, J. Urol. **54**: 1-9 (July) 1945.

3. Nation, E. F.: Horseshoe Kidney: A Study of Thirty-Two Autopsy and Nine Surgical Cases, J. Urol. **53**:762-768 (June) 1945.

cent) were women. Horseshoe kidney is approximately 38 per cent, or 2.6 times, commoner in men than in women.

Of the patients who were found at autopsy to have horseshoe kidneys which had not been apparent clinically, 45 per cent had had a blood pressure above 140 systolic and 90 diastolic in millimeters of mercury and 30 per cent had had a blood pressure above 170 systolic and 110 diastolic. The corresponding percentages of patients without horseshoe kidney were 45 and 15 respectively.

The range in weight of the horseshoe kidneys was from 230 to 550 Gm., the extremes deviating because of disease. The mean was 342.3 Gm. and the median and the mode were 300 Gm. Thirty-three of the patients had not complained of symptoms thought to result from the horseshoe kidney. In only 1 patient was death the result of apparent renal disease; in this case, the patient had malignant nephrosclerosis.

Nephritis was not found more commonly than expected in such a group of cases.

The author also reported 9 cases of horseshoe kidney in which operation was performed between 1934 and 1941. The ages of the patients ranged from 9 to 59 years. Seven of the patients were men, and 2 were women.

Five patients had a normal blood pressure, and 2 of the patients who had hypertension were cured by renal operation.

The symptoms complained of were the result of the pathologic processes rather than of the renal fusion. Pain was the commonest symptom.

Six of the 9 patients had renal calculi. The other 3 had obstruction and dilatation, with pyonephrosis.

In only 3 cases were symphysiotomy and nephropexy performed.

Five patients obtained partial or complete relief. The other 4 had progressive changes, and the results were poor.

Horseshoe kidney alone does not cause or predispose to hypertension. The average horseshoe kidney is slightly more than twice the size of a normal kidney. Horseshoe kidney is compatible with comfort and good health; it causes appreciable symptoms in a minority of cases. Most symptoms are caused by renal disease rather than by renal fusion.

Infection.—Heaney and Kretschmer,[4] in considering pyelitis of pregnancy, stated that in a series of 9,802 cases of pregnancy there were 31 cases of pyelitis, or an incidence of only 0.3 per cent.

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4. Heaney, N. S., and Kretschmer, H. L.: Pyelitis of Pregnancy: Foci of Infection in Its Prevention, J. A. M. A. **128**:407-408 (June 9) 1945.

Early studies disclosed that all patients with pyelitis of pregnancy had pronounced dilatation of the upper part of the urinary tract. Recently, Kretschmer and Heaney studied the urinary tract in 19 cases of normal pregnancy, by means of retrograde pyelograms. All the women were free of all signs and symptoms of infection of the urinary tract. In 47.36 per cent of the cases bilateral dilatation was found, and in 35.84 per cent the renal pelvis and ureter were dilated on one side only while in 15.8 per cent no dilatation was found. In 100 per cent of another series of cases, dilatation of the renal pelvis and ureter occurred during pregnancy and the puerperium. A striking feature of the dilatation was that it was almost uniformly above the brim of the pelvis. This study showed that dilatation is progressive with pregnancy.

In systemic diseases, bacteria frequently enter the blood stream through the kidneys and are eliminated through the urine. When the kidneys are sound and the urinary tract is open the organisms escape without injury of the urinary tract, but when obstruction to the urinary tract is present pyelitis may result. Pyelitis develops after acute colds and not infrequently during acute infectious diseases such as measles. In children's hospitals and orphanages, pyelitis commonly occurs after gastroenteritis. Pyelitis of pregnancy may occur after acute food poisoning. Heaney and Kretschmer reiterated the importance of the routine eradication of foci of infection in the preparation of women for expected pregnancy.

They made an analysis of the hospital records of the 31 patients who had pyelitis. In 2 cases the records were incomplete, and in 2 others no foci of infection were recorded, thus leaving histories of 27 cases for consideration in this study. There were 17 patients with one focus, 4 with two foci, 3 with three foci, 2 with four foci and 1 with five foci.

Heaney and Kretschmer said that pyelitis of pregnancy is a preventable disease or, if not completely preventable, the incidence of its occurrence can be reduced to a minimum.

Aneurysm.—Blain, Glynn and Hiratzka [5] reported a case in which a dissecting aortic aneurysm involved a renal artery and simulated acute nephrolithiasis. They stated that the literature contains reports of 15 cases in which a dissecting aneurysm of the aorta caused hematuria or other urologic symptoms. In most of the cases the symptoms simulated those of an acute urologic disease. In 9 of the 15 cases a correct diagnosis was made before autopsy. The authors reported

5. Blain, A., III; Glynn, T. P., and Hiratzka, T.: Dissecting Aortic Aneurysm Involving a Renal Artery and Simulating Acute Nephrolithiasis, J. Urol. **53**:753-761 (June) 1945.

a case in which the dissecting aneurysm involved the right renal artery and simulated acute right renal lithiasis. They cited a second case, in which a dissecting aneurysm involved the left renal artery and necessitated a consideration of acute left renal lithiasis in the differential diagnosis. In each case correct diagnosis and pathogenesis were suspected when the patients were admitted to the hospital.

Levine [6] stated that aneurysms of the renal artery are rare and that as far as he has been able to determine only 76 cases of this lesion have been reported in the literature. In 13 of these cases, the diagnosis was made before operation or before the patients died.

In the case which he reported the patient was a woman, aged 59 years, who complained of pain in her abdomen. A wreathlike calcific shadow situated medially to the right kidney and above the hilar notch was observed in the roentgenogram. As this finding is considered typical of an aneurysm, a diagnosis of aneurysm of the renal vessels was made. An exploratory operation revealed a pulsating mass just medial to the right kidney. The kidney and the aneurysm were removed. The aneurysm was approached transperitoneally, as it was considered advisable to ligate the renal vessels before the aneurysm was mobilized. As a precautionary measure, tapes were passed under the vena cava, above and below the renal vessels.

Carbuncle.—Shearer, Wiper and Miller [7] reported a case of renal carbuncle in which the patient was treated with penicillin. The patient had had pain in the renal area for two months. Surgical exploration did not disclose any lesion. Retrograde and excretory pyelograms later revealed that the middle and lower calices of the left kidney were smaller than normal and pushed to the right. Another exploratory operation was performed. An aspirating needle was passed into several suggestive areas, and purulent material was obtained from a site deep in the substance of the kidney at the junction of the upper two thirds and lower third. The cavity was opened and a catheter inserted. Penicillin was administered intramuscularly, and the abscess cavity was washed out with a dilute solution of this agent. The patient responded well to treatment; the wound healed, and healthy renal substance was conserved.

URETER

Papilloma.—Ottley [8] reported a case of benign papilloma of the ureter. The patient, a woman aged 71 years, had hematuria of

6. Levine, B.: Aneurysm of the Renal Artery, J. Urol. **54**:17-21 (July) 1945.

7. Shearer, T. P.; Wiper, T. B., and Miller, J. M.: Renal Carbuncle: A New Method of Treatment, J. Urol. **54**:12-16 (July) 1945.

8. Ottley, C. M.: A Case of Benign Papilloma of the Ureter, Brit. J. Surg. **32**:531 (April) 1945.

moderate degree. On cystoscopy, ureteral obstruction was found on the right side. Intravenous pyelography was performed, but none of the dye was excreted on this side. Nephroureterectomy was performed. There was a spindle-shaped enlargement at the lower end of the ureter. Histologic examination revealed that the lesion was a benign papilloma. The patient was alive and well three years later.

BLADDER

Cord Bladder.—Thompson [9] discussed the restoration of function of cord bladders by transurethral operation.

In some cases the cord injury may be minor in degree, and even though paralysis exists it is one sided or temporary in nature and normal micturition is disturbed either for a short period or not at all. In the majority of cases, paralysis is so extensive that micturition is impossible and remains so for many months.

In the early phase of the paralysis, the bladder of a few of the patients can be emptied by manual pressure applied in the suprapubic region. As time goes on, however, these few usually find that more and more pressure must be applied and that the bladder cannot be completely emptied. Finally, infection will develop, for infection follows stasis no matter where it occurs in the urinary tract. The majority of paralyzed patients require drainage of the bladder.

After a lapse of weeks or months, when the catheter is removed, some of the patients have what is loosely called an "automatic bladder." In other words, they void at irregular intervals but are usually incontinent to some degree; hence a urinal of some type must be worn at all times. Thompson has never seen a patient afflicted with cord bladder who could accurately time the period of automatic voiding, catch the urine as it is voided and stay dry between times. For this reason, drainage by catheter is usually continued indefinitely.

If the indwelling catheter can be dispensed with, the patient's condition improves rapidly and after a few months hospitalization is no longer required. This can be accomplished by transurethral operation. Many months must elapse, however, before any surgical procedure of this sort is attempted to restore micturition. Some patients will have spontaneous recovery of function which is satisfactory. But in the patients who are entirely unable to micturate after maximal recovery of neural function has taken place, a properly performed transurethral resection of the vesical neck will restore voluntary control of vesical function.

9. Thompson, G. J.: Cord Bladder: Restoration of Function by Transurethral Operation, U. S. Nav. M. Bull. **45**:207-214 (Aug.) 1945.

Transurethral resection of the vesical neck does not cure the nerve lesion; neither does it restore the bladder musculature to normal, but it does enable the patient to micturate and to be continent.

The ability to micturate or the lack of it depends on the balance between the retention mechanism, provided by bladder neck and urethral musculature, and the emptying mechanism, consisting in involuntary detrusor urinae muscle tone combined with the voluntary power exerted by the abdominal muscles and diaphragm. Cystoscopic examination in these cases, if it is made a number of months after injury, will reveal that the previously flaccid bladder wall has changed to detrusor muscle fibers, which are definitely hypertrophied. Trabeculation and sometimes cellule formation will be noted. Even though the vesical neck appears relaxed, it will be evident on careful examination that the muscle bundles which surround the vesical neck are also thickened. This is especially noticeable on critical examination when the bladder is distended.

In some instances a prominent contraction ring is apparent. It would seem highly probable that the contraction or stiffening of the musculature at the outlet prevents emptying of the bladder.

When a transurethral resection is performed, it is important to remove a substantial amount of tissue. The resection of a few pieces from the posterior half of the vesical neck usually accomplishes nothing; as a rule, tissue must be excised from the entire circumference of the outlet. Only in this way can the resistance of the retention mechanism be diminished sufficiently so that an increase of pressure within the abdomen, accomplished by straining, will squeeze the bladder dry.

The most gratifying feature of all is that between periods of micturition the patients have perfect control. Depending on fluid intake, four or more hours may elapse between periods of micturition.

Fistula.—Wilhelm's [10] experience indicates that rectourinary fistulas caused by trauma or acute inflammation often heal with conservative treatment. On the other hand, those due to tuberculosis or neoplasm offer a grave prognosis. Short traumatic fistulas of large diameter are apt to persist and to require radical operative repair. These chronic rectovesical and rectourethral fistulas are usually best approached by the perineal route. Fecal diversion is valuable as palliative treatment and may occasionally be followed by spontaneous closure of a fistula. However, the preoperative administration of succinylsulfathiazole has enabled us to dispense with colostomy preliminary to radical repair. In 9 of the 13 cases of rectourinary fistula, the patients were cured; in another case, the patient was greatly improved.

10. Wilhelm, S. F.: Treatment of Recto-Urethral and Recto-Vesical Fistula, J. Urol. **53**:719-722 (May) 1945.

Carcinoma.—Hayes and Segal [11] considered mucinous carcinoma of the urachus, which invades the bladder, and they reviewed 44 cases collected from the literature and reported 1 case which they had observed. The majority of the patients were men, and all were in the middle and later periods of life. The youngest patient was a man 26 years old. In all but 1 of the reported cases, the neoplasm had eroded through the vesical mucosa. Cystoscopy revealed either a fungating ulcer or a papillary mass of varying size at the vault of the bladder.

In the case which they reported, the patient was a man, aged 65 years, who complained of pain in the lower part of the back and painless hematuria. Cystoscopy revealed a papillomatous growth in the fundus of the bladder, a part of which was resected with the McCarthy resectoscope. Two weeks later, the bladder was opened and the mass, which was found to be attached to the peritoneum, was removed. The diagnosis was adenocarcinoma of the urachus, which had perforated the urinary bladder.

Ulcer.—In the investigation of the lymphatics of the bladder, Powell[12] was impressed by the similarity of the microscopic picture of progressive chronic lymphatic edema and the classic histologic description of Hunner's ulcer.

The author successfully injected the lymphatics of the bladders in 24 infant cadavers. From this study he concluded that there was a bottleneck of the lymphatics coming from the dome of the bladder. Powell stated that lymphatic blockage was possible in the female but not likely in the male. Should blockage ensue, a lymphedema of the mobile portion of the bladder would be expected and a physiologic vicious cycle put into action, in which edema, spasm and nutritional disturbance at the surface of mucosa would inevitably follow, as is known to occur in Hunner's ulcer. The author outlined possibilities of the lymphatic block as follows:

1. Blockage of a large number of lymph nodes by infection.
   a. Pelvic inflammatory disease now or at some time in the past (specific or nonspecific).
   b. Various types of inflammation as a result of normal or abnormal parturition, abortion, ovarian disease, chronic cervicitis, etc.
   c. Infections in the cul-de-sac, retroperitoneal from perinephritis, etc., peritonitis and proctitis [lymphopathia venerea].
2. Interruption of lymph circulation by tumors, such as fibroids and other pelvic surgical diseases.

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11. Hayes, J. J., and Segal, A. D.: Mucinous Carcinoma of the Urachus Invading the Bladder, J. Urol. **53**:659-669 (May) 1945.

12. Powell, T. O.: Studies on the Etiology of Hunner Ulcer, J. Urol. **53**:823-835 (June) 1945.

3. Surgical interruption of collectors during pelvic operations.
4. Blockage of anterior horizontal collectors.
   a. By infection as a result of cervicitis, giving rise to supravesical fibrosis.
   b. By possible pressure from uterus against pubic bone, interrupting rare type of main collector on the anterior wall of bladder.

On reviewing all the reported cases in the literature, the author concluded that careful evaluation revealed that the majority of patients suffer or have suffered from gynecologic disease or a disease process in the region of the rectum or that they have undergone some operation on the pelvis or lower part of the abdomen.

Powell further stated that the histologic sections of dogs' bladders with partial lymphatic obstruction were not unlike those in the majority of reported cases of elusive ulcer. The pathologic process can be better appreciated grossly at the time of operation than later, when the tissues are fixed and shrunken. The history in most instances indicates a chronic process over a long period, averaging five to ten years. Probably the majority of patients with the same early history overcome their lymphatic disturbance and recover. Only in the rare case in which several mechanisms come into play does the blockage cause Hunner's ulcer.

Incrustation.—Lins [13] described a primitive method of dissolving the skeleton of the Candiru, which permeates the urethras and bladders of bathers in the Amazon. This remedy is the buitach apple made into a brew and drunk hot. A synthetic formula similar to the brew from the buitach apple was given; this consists of methenamine 10 Gm., proteolytic enzyme (pepsin) 1 Gm., citric acid 32 Gm., tannic acid 10 Gm., magnesium oxide 4 Gm., sodium carbonate 4 Gm. and water 1,000 cc. In 12 cases of vesical incrustation and alkaline cystitis in which this formula was employed, all the calcareous material in the bladder disappeared.

Herger and Sauer [14] stated that their investigations as to the usefulness of the stone-dissolving agent known as solution G (a solution of citric acid, magnesium oxide and sodium carbonate of p_H 4) have indicated that it is a valuable adjunct in the treatment of persistent alkaline infections of the urinary tract. It is of particular value in cases in which a tendency toward formation of stones and incrustation is predominant. In none of the 41 patients treated has the use of solution G produced ill effects of appreciable importance, and it was tolerated by all patients who were able to tolerate an indwelling catheter.

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13. Lins, E. E.: The Solution of Incrustations in the Urinary Bladder by a New Method, J. Urol. **53**:702-709 (May) 1945.

14. Herger, C. C., and Sauer, H. R.: Treatment of Alkaline Incrustations of the Urinary Tract with Solution G, J. Urol. **53**:696-701 (May) 1945.

The results accomplished were most impressive in cases of incrusted alkaline cystitis and in cases of incrusted radium necrosis. Owing to its ability to dissolve calcareous deposits consisting of alkaline phosphates, it is considerably superior to other methods heretofore employed in the treatment of these conditions. The experience of Herger and Sauer has shown that in the majority of cases one course of treatment, lasting from two to four weeks, has been sufficient to produce lasting results; however, in certain cases it will be necessary to repeat treatment if manifestations of recurrent disease develop.

As to the value of solution G as a stone-dissolving agent, they found that it was indicated under certain conditions only.

Solution G has proved valuable in cases in which formation of stones in the kidney occurs as a result of infection with urea-splitting bacteria. Heretofore, surgical removal of these concretions was the only alternative. By the use of solution G, it is within the realm of possibility to dissolve these stones before they become hard or before they attain large size. If surgical removal of stones from badly infected kidneys is carried out, nephrostomy should be done routinely in order to facilitate postoperative irrigation with solution G. Also, in cases of sandlike deposits or multiple calculi in the renal pelvis in which complete removal of concretions is impossible without severely injuring the kidney, Herger and Sauer advocated the use of solution G postoperatively for a dual purpose, namely, to dissolve the remaining stones and to prevent formation of new stones.

The indication for use of solution G for the purpose of dissolving vesical stones is a limited one. Since many of the patients require elimination of some form of obstruction, surgical procedures are preferable to a tedious and time-consuming attempt at dissolution of the calculi. Even in cases in which there is no evidence of obstruction, litholapaxy or removal of small stones with the aid of the rongeur is a much simpler procedure. However, the use of solution G should be advocated under certain conditions, namely, in the cases of alkaline vesical stones in which the patients refuse operation or transurethral manipulation, in cases in which such procedures are contraindicated for various reasons and in cases in which the bladder is so badly infected that treatment of the infection is desirable before attempts at removal of vesical stones are made.

PROSTATE GLAND

Hypertrophy.—Nesbit [15] made an evaluation of clinical data in 176 cases of "large" prostate glands treated by transurethral resection at the University Hospital of the University of Michigan Medical School.

15. Nesbit, R. M.: Transurethral Resection for Prostatic Hypertrophies of Large Size, Surg., Gynec. & Obst. **81**:515-520 (Nov.) 1945.

This study disclosed that the size of the gland was not a determining factor influencing the morbidity, mortality or length of stay in the hospital. Comparison of data in this group of cases with those of all cases of benign hypertrophy revealed that the loss of blood is greater when the large glands are resected and, as a result, postoperative transfusions are more often required; also, that external urethrotomy is done more often in this group of cases (33.5 per cent) than in all cases of resection (20 per cent).

The end results following transurethral resection in this group of cases are excellent; in only 1 case was the result regarded as poor. The end results in cases in which more than 80 Gm. of tissue were removed were just as good as those in the other cases in this group, and these facts support the impression that has long prevailed among experienced resectionists, namely, that patients with large prostate glands obtain just as good results following a proper resection as do patients having smaller prostates and that the end result following transurethral resection is determined not by the size of the prostate but rather by the adequacy of its removal.

Bassow [16] reported a case in which progressive gangrene of the skin followed suprapubic prostatectomy. He stated that this condition is a rare postoperative complication. Its cause is not clear. It may occur in the young patient as well as in the old one. Surgical technic does not appear to be an etiologic factor. Physical debility is of questionable significance when one considers the large number of elderly debilitated persons who undergo operation and who apparently escape this particular surgical complication.

That this complication is even less frequent in urologic surgical treatment than in general operation may perhaps be explained by the increased use of the transurethral approach to the obstructing prostate and the less frequent use of the suprapubic technic. Furthermore, prostatism, which is an insidious symptom complex, may stimulate an appreciable resistance to the infectious organisms, which are ever present in large numbers.

The case reported by the author was studied in retrospect only. Had the lesion been identified earlier and had more radical treatment been instituted, death might have been averted. The clinical appearance of the lesion, the symptom complex associated with the disease, such as excruciating local pain, the absence of systemic reactions and the cultural identification of the two organisms acting in a symbiotic arrangement removed all doubt as to the correct classification of the lesion.

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16. Bassow, S. H.: Postoperative Progressive Gangrene of the Skin Following Suprapubic Prostatectomy, J. Urol. **54**:46-52 (July) 1945.

Hey [17] discussed the principles of aseptic suprapubic total prostatectomy. It was suggested that postoperative uremia is due to infection and is encouraged by any method of slow decompression, open drainage or instrumentation. Slow decompression in chronic obstruction is unnecessary. The importance of avoiding a septic procedure and of not leaving a permanently infected urinary tract in an old man was stressed. "Aseptic prostatectomy" should reduce the over-all mortality by at least 80 per cent.

Carcinoma.—Nicholson [18] reported a case of carcinoma of the prostate in which the patient was 15 years old. He had had difficult micturition and retention of urine. Rectal examination with the bladder empty disclosed a hard, nodular prostate. An intravenous urogram showed bilateral hydronephrosis. A plain roentgenogram of the abdomen and pelvis disclosed nothing abnormal. A suprapubic cystostomy was done, and a mass about the size of a tennis ball was found in the region of the prostate. It was nodular and hard. The patient died the following day.

Gardiner and Cummins discussed a similar case, in which the duration of symptoms was even shorter; the patient died seven weeks after the onset of symptoms.

PENIS

Anomalies.—Blanco [19] reported a case of diphallus, or double penis. The two organs had a common covering on their posterior parts but were completely independent and free anteriorly. The upper and normally developed penis was functionally perfect, while the lower and smaller one acted as a supernumerary penis and had no function whatever. Although each penis appeared to have its individual urethra, it could not be determined whether there was a union between them or whether there were two completely independent urethras communicating with a common bladder. With the exception of a divided scrotum, no other anomalies were found either in the genitourinary tract or elsewhere in the body. It is unfortunate that, owing to lack of cooperation on the part of the patient, Blanco was unable to present a complete study of this interesting case.

URETHRA

Glandular Structure.—Folsom and O'Brien [20] said that the posterior part of the female urethra is surrounded by a definite group of glands which are identical with the prostate gland in shape, distribution,

17. Hey, W. H.: Asepsis in Prostatectomy, Brit. J. Surg. **33**:41-46 (July) 1945.

18. Nicholson, N. J.: Carcinoma of the Prostate in a Youth, Brit. J. Surg. **32**:533-534 (April) 1945.

19. Blanco, S.: Diphallus (Double Penis), J. Urol. **53**:786-790 (June) 1945.

20. Folsom, A. I., and O'Brien, H. A.: The Female Urethra: The Connecting Link Between the Urologists and the Gynecologists, J. A. M. A. **128**: 408-413 (June 9) 1945.

secretory activity and site. These glands may become infected in early infancy and may remain infected for many years or even throughout life. Such infection may produce a varied and at times a bizarre papillary posterior urethritis. This inflammatory urethritis may vary from a mild granular urethritis to a more definite papillary urethritis.

In many cases the urethral lumen is definitely narrowed and the stricture is part of the pathologic picture.

There are two groups of clinical symptoms that are produced by this inflammatory posterior urethritis, namely, vesical irritation and pain. Many women suffer for years from either a continuous or a frequently recurring vesical irritation characterized by urinary frequency and burning. These symptoms vary widely in different cases; some women are merely annoyed by occasional attacks of a mild degree, while others may have almost a constant urinary frequency and burning. At least 90 per cent of the women who have a urologic disease have this vesical irritation as one of the presenting symptoms if not the main one. In 90 per cent of this group an inflammatory urethritis is the cause of this troublesome symptom. In spite of this, the urine is usually free from pus.

Another symptom of this inflammatory posterior urethritis is pain. The pain is referred to various sites. As a rule it is dull and aching in character, but at times it may be similar to renal colic in its site and severity.

The most frequent sites of this referred pain are the lower part of the iliac region, the lumbosacral region, the loin and the inner side of the thigh. If the pain is severe and situated in the loin, it may be mistaken for the pain of renal or ureteral disorder.

Urethral dilation should be performed regularly twice a week. At first, one should use a sound that will stretch but not tear the urethral mucosa. Then the size of the sound should be gradually increased until a 30 or 32 F. can be inserted easily. After each dilatation, 10 to 15 cc. of a 0.25 per cent solution of strong protein silver should be instilled into the urethra. When the urethra has been dilated for about six weeks, one should fulgurate some of the pathologic tissue in the posterior urethra. The patient then should be allowed to rest for two weeks. Then performance of dilation should be resumed for from six weeks to two months; at the end of this period, fulguration should be repeated. This routine should be continued until the patient is relieved and there is no further evidence of pathologic change in the posterior urethra.

Diverticula.—Higgins and Rambousek,[21] in discussing diverticula of the female urethra, stated that the classification of any diverticulum as

21. Higgins, C. C., and Rambousek, E. S.: Diverticula of the Urethra in Women: Review of Twelve Cases, J. Urol. **53**:732-738 (May) 1945.

acquired or congenital is modified by the duration of symptoms, method of onset, age of the patient and histologic character of the lesion. Congenital diverticula are apparently rare; a review of the literature reveals only 2 cases of this type. The lesion probably results from infection of the urethral glands, with sealing of their openings into the urethra. An abscess develops and ruptures into the urethra, reestablishing the communication. This appears to have been the sequence in all but 1 of the 12 cases reported by these authors. Acquired diverticulum may be secondary to urethral stricture or stone, or it may follow instrumentation of the urethra. It is frequently asserted that trauma sustained by the urethra during childbirth may produce a diverticulum.

The symptoms may be localized or referred to the urinary tract. When the symptoms are localized, the patient may complain of pain, a tender mass, dyspareunia and recurrent discharge of pus from the urethra, which is followed by relief. The three commonest symptoms in the case reported by Higgins and Rambousek were dysuria, discharge of pus from the urethra, with relief of symptoms, and the presence of a palpable mass.

The diagnosis should be considered whenever women complain of symptoms in the lower part of the urinary tract, particularly of recurrent attacks of cystitis for which there is no other explanation. When the patient complains of a mass in the region of the urethra, which may be tender and painful to touch, diverticulum should always be suspected, especially when the symptoms subside after discharge of pus from the urethra. The expression of purulent material from the urethra by digital pressure through the vagina over the painful mass is practically pathognomonic. The diagnosis is established by careful palpation of the urethra, urethroscopic examination and urethrography.

Most urethral diverticula have thick fibrous walls and show evidence of chronic inflammation. In 16 of 24 reported cases, the lining membrane consisted of squamous, columnar, cuboidal, transitional and stratified squamous epithelial cells. In the other 8 cases, a lining membrane was absent but the inner surface of the sac consisted of granulation and fibrous tissue.

Higgins and Rambousek reported 12 cases of urethral diverticula observed at the Cleveland clinic. In all but 1 of the cases the diverticula were obviously of the acquired type, since they occurred in women between the ages of 38 and 66 years. The duration of symptoms ranged from five months to eleven years. All but 2 of the patients gave a history of recurrent attacks of cystitis, and all had painful masses in the region of the urethra at some time during their illness. Five of the patients were completely cured by excision of the diverticulum. In 1 case, incision and drainage of the infected diverticulum produced satisfactory results. Two patients responded satisfactorily to drainage of

the diverticulum by frequent digital pressure and urethral dilation. In 2 instances treatment was not recommended, as the patient had no symptoms referable to the diverticulum. A postoperative urethrovaginal fistula developed in 2 of the 5 cases in which the diverticulum was excised. In 1 of these cases, the fistula was closed and the patient remained asymptomatic. In the other case, a minute fistula was noted at examination three years after the excision, although the patient was unaware of its presence.

McNally,[22] in discussing diverticula of the urethra, stated that he had observed 5 cases and had collected 6 more from hospital records. In 9 of the 11 cases there was a history of a suburethral abscess, and in 2 of these cases the patients were first seen when the abscess was present and later were seen again when the diverticulum was present. The diagnosis is simple if one considers and remembers the fact that a diverticulum can be present.

McNally found no case in which symptoms were absent, and he expressed the opinion that the diverticulum should be excised. Excision has been a fairly simple procedure in his hands. He uses a prostatic retractor to retract the urethra. The vaginal incision is made to one side of the diverticulum, the diverticulum is excised and the sac is transfixed and ligated. Some tissue is brought over the neck of the sac, and the vaginal incision is closed to one side, so that the incisions are staggered. McNally has not observed a urethrovaginal fistula in any of his cases.

Downer and Virgilio[23] reviewed the literature on diverticulum of the female urethra and reported a case which they had observed. This urologic entity would become commoner than one is led to believe if every case that came under observation would be reported. Exact statistics as to the frequency of this lesion are not available. In the vast majority of the cases the lesion is acquired from either inflammatory processes or trauma. The literature contains reports of cases in which the lesion has been believed to be congenital. Downer and Virgilio reported a case in which the lesion was acquired and of infectious origin. Diagnosis is not difficult if the condition is borne in mind. It may be made absolute by urethroscopy and urethrography. Excision of the sac is the treatment of choice and results in prompt relief of symptoms.

Carcinoma.—Hess[24] stated that cancer of the female urethra is a preventable disease if granular urethritis is recognized and treated. All

22. McNally, A., in discussion on Higgins and Rambousek,[21] p. 739.

23. Downer, I. G., and Virgilio, F. D.: Diverticulum of the Female Urethra: Review of Literature with Case Report, J. Urol. **54**:53-58 (July) 1945.

24. Hess, E.: Primary Carcinoma of the Female Urethra, with Especial Reference to the Lesion Known as Urethral Caruncle, Pennsylvania M. J. **48**: 1150-1155 (Aug.) 1945.

hyperplastic lesions of the mucosa of the female urethra must be considered malignant until proved otherwise by biopsy. The majority of these conditions—mucosal hypertrophy with eversion, external and internal caruncle and the suspected malignant lesion—usually affect women who are between 40 and 70 years and who have had genital infection for a long time. The percentage of cases in which these hyperplastic lesions become malignant is much larger than ordinarily considered, that is, approximately 33 per cent. Involvement of the lymph nodes, which usually occurs late in the course of the disease, is a bad prognostic sign. In cases in which there is extensive infiltration of the anterior wall of the vagina, the author transplants the ureters into the skin or intestine. This procedure is followed by total cystectomy and the removal of a large portion of the anterior wall of the vagina.

CHEMOTHERAPY

Penicillin.—Nolan [25] stated that penicillin is an addition to other types of urologic treatment and not a substitute for any recognized surgical procedure. Used alone or in conjunction with surgical treatment, it is a most important addition that will result in a reduction in mortality and morbidity. Its field of use is limited to cases in which the organisms are specifically sensitive to it, and it will even then not affect those organisms if it cannot reach them because of the presence of foreign bodies, necrotic material, avascular tissues or lack of drainage.

Because of the high concentration in the urine, the prolonged use of penicillin may be indicated in cases in which infection is due to some organism that is not particularly sensitive to this substance. The optimal time-dose ratio must be based on the sensitivity of the organism and on the severity and site of the infection. Penicillin, like the sulfonamide drugs, should be administered in relatively large doses initially, so that the micro-organisms have no chance to become resistant. The minimal degree of toxicity renders this course harmless. Penicillin is much better tolerated than are the sulfonamide compounds.

Staphylococci require, as a rule, much larger doses of penicillin than do susceptible strains of streptococci. Nolan advocated large initial doses, with proper time ratio, to prevent the organisms from becoming resistant to penicillin. In cases of severe staphylococcic infection, a total dose of between 1,000,000 and 3,000,000 units should be administered and the treatment should be continued from ten days to two weeks to produce maximal therapeutic results.

After a study of the oral administration of penicillin with various enteric coatings and adjuvants to protect the penicillin or promote its

25. Nolan, O. F.: Treatment of Genito-Urinary Tract Infections with Penicillin, J. Urol. **53**:817-822 (June) 1945.

absorption, Cutting, Halpern, Sultan, Armstrong and Collins [26] recommended the following useful combinations: mixtures of penicillin with triisopropanolamine, trisodium citrate or sodium carbonate enclosed in a resin-cellulose plastic enteric coating.

When a dose of 50,000 units of penicillin was administered every two hours until ten doses had been given, these combinations produced concentration of from 0.02 to 0.05 units of penicillin per cubic centimenter of blood. Fifty-three patients who had acute gonorrhea were treated with several of the most promising combinations. A cure was obtained in 38, or 72 per cent, of the 53 cases. Oral administration of penicillin appears practicable in cases of infection with bacteria that are highly susceptible to this substance.

Romansky, Murphy and Rittman [27] reported a series of 175 cases of gonorrhea in which the patients, who were men, were treated by a single injection of calcium penicillin in a mixture of yellow wax and arachis (peanut) oil. The results were satisfactory in all the 75 cases in which a single injection of 150,000 units was employed. Ninety-three of the 100 patients who received single injections of 100,000 units were cured. The remaining 7 responded to a second single injection of 150,000 units of penicillin in the mixture of yellow wax and arachis oil.

A single injection of 100,000 to 150,000 units of calcium penicillin in yellow wax and arachis oil will produce and maintain essayable levels of penicillin in the blood for seven and a half to ten hours, and excretion of penicillin in the urine will continue for twenty-four to thirty-two hours.

The administration of penicillin in a mixture of yellow wax and arachis oil has not produced any abnormal reactions either locally or constitutionally.

Cohen and Grover [28] studied several plans of administering penicillin to ambulatory patients and reported their results. A single intramuscular injection of 100,000 units of penicillin in aqueous solution is not efficacious in the treatment of gonorrhea in men. It produced a cure in only 41.4 per cent of the cases in which it was used. Divided doses of penicillin are more effective than single large doses, provided the time interval between doses is neither too long nor too short. In cases in which treatment has not been employed previously, the addition of

26. Cutting, W. C.; Halpern, R. M.; Sultan, E. H.; Armstrong, C. D., and Collins, C. L.: Administration of Penicillin by Mouth, with Results in the Treatment of Gonorrhea, J. A. M. A. **129**:425-432 (Oct. 6) 1945.

27. Romansky, M. J.; Murphy, R. J., and Rittman, G. E.: Single Injection Treatment of Gonorrhea with Penicillin in Beeswax-Peanut Oil: Results in 175 Cases, J. A. M. A. **128**:404-407 (June 9) 1945.

28. Cohen, D. L., and Grover, M. L.: Ambulatory (Duty Status) Sodium Penicillin Therapy of Gonorrhea in the Male, J. Urol. **53**:812-816 (June) 1945.

sulfathiazole to penicillin will increase the percentage of cures obtained. Sulfonamide-resistant gonorrhea also shows a tendency to be resistant to penicillin. Beyond a certain point, probably about 50,000 units, an increase in the size of a single dose rapidly invokes the law of diminishing returns. It is believed that in the not too distant future "penicillin-resistant" gonorrhea, analogous to "sulfonamide-resistant" gonorrhea, will be encountered. Local penicillin therapy by means of intraurethral instillation for periods of one hour is of no value in the treatment of gonorrhea.

Koch, Haines and Hollingsworth [29] made a study of the value of penicillin in the treatment and control of gonorrhea. Of 485 patients treated with an initial course of 200,000 units, 68 (14 per cent) were not cured. Hospitalization of patients with gonorrhea does not appear to affect the rate of failure. This would indicate that failures occurring in outpatients are probably not reinfections. Minimal criteria of cure, including multiple cultures in penicillin-treated patients with gonorrhea, are indispensable to the public health control of the disease.

The authors found no case of complete penicillin resistance; however, in 1 of 7 cases the result of the first course of treatment was a failure. In many cases more than two courses were required, and in some of the cases sulfonamide drugs and pyrotherapy were administered simultaneously.

The authors were unable to comfirm the necessity for the usually accepted practice of differentiating gonococci and other members of the Neisseria family by sugar fermentation tests; three hundred and fifty laboratory observations, although not conclusive evidence, constitute a considerable group on which to base an opinion.

In the control of gonorrhea, the medical profession must be aware of the limitations of penicillin therapy, the possibility of producing a carrier state and the social factors related to the spread of the disease.

Sulfonamide Drugs.—Lehr [30] made a comparative study of the acute and chronic toxicity of the sodium salts of sulfacetimide, sulfadiazine and sulfanilamide by administering these drugs intraperitoneally to albino rats.

Figured on the basis of the median lethal dose (LD_{50}), sodium sulfacetimide possesses by far the lowest acute toxicity, being about five times less toxic than sodium sulfadiazine and more than seventeen times less toxic than sodium sulfanilamide. Based on mean values

29. Koch, R. A.; Haines, J. S., and Hollingsworth, W. Y.: Evaluation of Pencillin in Gonorrhea Treatment and Control, J. A. M. A. **129**:491-495 (Oct. 13) 1945.

30. Lehr, D.: Experimental and Clinical Studies with Sulfacetimide (p-Aminobenzenesulfonylacetylimide): Toxicity and Efficiency in Bacillary Infections of the Urinary Tract; I. Experimental Studies, J. Urol. **54**:87-105 (July) 1945.

of the highest concentration of these drugs in the blood after the administration of fatal doses of the three sulfonamide drugs, the relationship of the acute toxicity of sulfacetimide, sulfadiazine and sulfanilamide is as 1 : 2 : 10.

The chronic toxicity of sodium sulfacetimide is likewise by far lower than the toxicity of sodium sulfadiazine. When a daily dose of 0.6 Gm. per kilogram of body weight was administered for nine weeks, sulfacetimide caused no significant pathologic lesions. The equimolar amount of sulfadiazine (0.7 Gm. per kilogram), however, invariably produced severe organic damage, particularly in the kidneys and, in many instances, also in the aorta.

The low renal toxicity of sulfacetimide was explained as due to its high solubility (in water, sulfacetimide is about one hundred and fifteen times as soluble as sulfadiazine), which apparently precluded the serious consequences of massive and long-lasting intratubular deposition of crystals which occurred when sulfadiazine was used.

The ready absorption and rapid renal elimination of sulfacetimide as well as its high solubility, particularly in urine, made it possible to obtain high concentrations of the drug in the urine in the presence of relatively low concentrations in the blood.

In in vitro antibacterial experiments, it was found that sulfacetimide exerted a powerful effect against Escherichia coli, even if extremely large inoculums were used.

The results of these experiments suggest that from a pharmacologic and toxicologic standpoint sulfacetimide deserves preference over other sulfonamide drugs now in use for the treatment of infections of the urinary tract.

FILARIASIS

McMartin [31] stated that filariasis has infected thousands of men in our armed forces in the Pacific Area. The disease in these men is characterized by episodes of lymphangitis and lymphadenitis. The majority of the patients have genital (scrotal) involvement. Civilian urologists will be confronted with the problems of differential diagnosis of intrascrotal pathologic changes caused by filariasis as well as intrascrotal pathologic changes usually encountered in the United States. There are many members of our armed forces who have filariasis and fear the onset of elephantiasis despite attempts of medical officers to dispel their fears. One can do a great deal to ease the minds of these patients by educating them on the characteristics of the disease.

There is no specific drug in the treatment of filariasis. Removal of the patient to a temperate climate and away from the chance of additional

31. McMartin, W. J.: Urological Aspects of Filariasis, J. Urol. **54**:62-74 (July) 1945.

infection is most important. Rest, elevation of the affected parts and cold applications are the treatment of choice in episodes of exacerbations of the disease. Research on the treatment of filariasis is constantly being carried out by competent medical personnel of the Army and Navy. Excellent results of this work soon may be reported in the literature. Much will be added to the knowledge of the pathologic changes of early filariasis when and if complete postmortem examinations can be done on patients who have filariasis or who have a history of having had filariasis at some time during their life.

Filariasis will not become a public health problem in the United States. Permanent disability as a result of filarial infestation among our armed forces will be a rarity. The Army and Navy Medical Corps have progressed rapidly toward eradication of this disease.

URINARY OBSTRUCTION

Urinary obstruction[32] involving most frequently the upper part of the ureter, the neck of the bladder and the urethra is a common lesion among the Army personnel. The acquired prostatic lesions of old age are uncommon, as might be expected. The majority of these lesions have existed prior to the patients' induction. Narrowing of the vesical outlet owing to fibrosis or muscular hypertrophy is frequently seen. The contracture may be a superficial sclerosis of the vesical neck without adnexal involvement or it may be deep seated from long-standing associated chronic posterior urethritis and prostatovesiculitis.

These contractures may be separated clinically into three groups, depending on the degree of sclerosis and obstruction. Group 1 includes vesical irritation, characterized by increased frequency of micturition, urinary urgency or nocturia and clear urine. Group 2 includes the stage of residual urine, with signs of obstructive uropathy in the bladder, such as trabeculation and hypertrophy of the trigone; there is diminution in size and force of the urinary stream and there may be associated sexual symptoms, such as premature ejaculations, persistent erections from posterior urethral irritation and sexual neurasthenia. During acute exacerbations, the urinary symptoms become more pronounced and there may be associated suprapubic and perineal discomfort, backache, renal colic or hematuria. Group 3, or the third stage, includes more advanced retention, with increasing inability to void, associated with periods of acute complete retention.

Careful routine urologic examination will permit one to make the diagnosis. Cystoscopy shows a deep urethral, vesical neck, changes

32. Riba, L. W., and Schmidlapp, C. J.: Surgical Treatment of Urinary Obstruction in Army General Hospital, Surg., Gynec. & Obst. **80**:368-372 (April) 1945.

in the trigone and vesical wall and elevation of the posterior vesical lip, with a characteristic deformity of the vesical outlet. Rectal palpation of the vesical neck while the instrument is in place in the urethra will show the degree of thickening of the posterior commissure. Cystourethrograms are valuable in demonstrating constriction of the vesical neck and associated changes in the bladder. When symptoms of vesical irritability are relieved temporarily after cystoscopic examination, a contracture should be suspected.

In cases of a mild degree of obstruction, treatment should be conservative and should include rest in bed, sedatives, heat and dilatation of the vesical neck. After the obstruction has reached the second stage, that of residual urine or retention, transurethral resection is indicated. Palliative treatment produces only temporary relief. Varying amounts of tissue have to be removed, from 5 to 20 Gm., depending on the depth and the degree of the obstruction.

Obstruction at the ureteropelvic junction is the commonest lesion of the upper part of the ureter and produces varying degrees of hydronephrosis. This lesion is congenital and usually is silent until infection or calculi or both have developed. Treatment is primarily surgical, and the well known principles regarding the selection of patients for operation and the type of surgical repair at the ureteropelvic junction are employed.

Urethral strictures were found in 12 per cent of the patients admitted to the genitourinary service of a large Army hospital. Strictures of wide caliber, that is, larger than 20 F., are usually asymptomatic, except for the slight morning drop, mild pyuria and shreds in the first glass of urine. They frequently respond to a repeated urethral dilation. The small caliber of multiple anterior urethral strictures presents more of a problem of treatment from the military standpoint. Such strictures usually occur in a soldier who has had repeated gonorrheal infection and a recurrent urethral discharge. There are usually an associated prostatovesiculitis and chronic or recurrent epididymitis. When acute gonorrhea or trichomonas infestation is superimposed on severe strictures, the infection usually is resistant to sulfonamide drugs and penicillin. In strictures of small caliber, progressive urethral dilation is indicated or if they are fibrous and resilient and respond poorly to dilation internal urethrotomy should be performed, preferably electrourethrotomy.

If in maladjusted or inadequate service patients the lesions existed prior to induction operation should not be performed unless emergency treatment is necessary. Operation performed on a soldier who cannot be rehabilitated may facilitate later pension claims.

Intrinsic ureteral strictures were found to exist in 2 per cent of a large series of cases in which urologic examination was performed.

These strictures were relatively asymptomatic until sufficient obstruction developed to invite infection. Care must be taken in interpretation of the ureterograms, for ureteral blockage to a catheter, nonopaque calculi, mucosal pockets, lateral angulation or spasm are frequently erroneously diagnosed as a stricture. Intrinsic neuromuscular dysfunction and ureteral dilatation resulting from chronic infection frequently suggest stricture on pyelography. In such cases, ureteral calibration is of value and will rule out the presence of an intrinsic stricture. The treatment is progressive ureteral dilation and the clearing-up of any coexisting infection.

In general, it may be said that in the Army there is ample opportunity to apply principles of recognized conservative measures in the treatment of urinary obstruction, which usually affects younger men. These procedures not only will rehabilitate the patients during the emergency but will in a great measure add to their health and happiness after their discharge from the service.

ENURESIS

Forsythe and Karlan [33] stated that in cases of enuresis examination should include careful neurologic and laboratory study and complete urologic examination. A cystometric study should be a routine procedure. In 13 of 25 cases studied, the enuresis was due to local uropathy; in 9 cases the patients had an uninhibited neurogenic bladder. In only 3 cases did the enuresis appear to be functional. Minor corrective urologic procedures often eliminate enuresis of long duration. The authors concluded that in most cases in which the patients are adults the enuresis probably is not functional in origin.

HEMOSPERMIA

Acute hemospermia is not uncommon, and the causes are often obvious, such as prostatitis and infection of the posterior urethra, vesical outlet and seminal vesicles. It also may be present in ejaculations following trauma or before there is complete healing following prostatic resection. Huggins and McDonald [34] consider hemospermia to be chronic if it persists for more than a month and if an obvious cause cannot be found.

In the past year they observed 9 cases of hemospermia. In 2 of the cases, symptoms had been present less than two weeks and disappeared spontaneously. In 5 of the cases, the semen had been bloody

33. Forsythe, W. E., Jr., and Karlan, S. C.: Enuresis in Young Male Adults, J. Urol. **54**:22-38 (July) 1945.

34. Huggins, C., and McDonald, D. F.: Chronic Hemospermia: Its Origin and Treatment with Estrogen, J. Clin. Endocrinol. **5**:226-231 (May-June) 1945.

persistently for one year or more. In the 2 remaining cases the symptoms had been present for one month and five months respectively. Urologic examinations did not disclose any gross abnormalities except prostatitis, which was present in 1 case. The 7 cases were selected for study because the cause of the hemospermia was unknown and successive bloody ejaculations had been present for a long time.

Fractionated collections of the semen as ejaculated were made in three glasses, and when the volume was small the semen was collected in a single tube. Chemical study consisted in the determination of reducing substances and the amount of fibrinolysin and acid phosphate. Microscopic examination of the semen in each glass was done to determine motility and shape of the sperm, and erythrocyte and spermatozoa counts were made in a counting chamber.

Gross examination of the fractionated semen collected in three glasses showed little or no blood in the first glass and progressively greater amounts of blood in the second and third glasses. In the same way, the concentration of glucose, a component arising from the seminal vesicle, was found to be greatest in the third glass, whereas the concentration of the prostatic derivatives, fibrinolysin and acid phosphates, was greatest in the first glass.

No erythrocytes were found in normal semen, although leukocytes and epithelial cells were always observed in small numbers. In cases of hemospermia, erythrocytes were always present, both singly and in agglutinated clumps. Results of cystourethroscopic examination of the patients were uniformly negative. On the basis of these observations, it is certain that hemorrhage arose in the seminal vesicle in all these cases of chronic hemospermia.

Estrogen in the form of ethinyl estradiol was administered orally to 6 patients with chronic hemospermia in doses of 0.05 mg. three times a week to twice daily, depending on the response. Treatment was continued three to seven weeks except in 1 case, in which it was obviously ineffective. A low dosage of ethinyl estradiol caused complete cessation of hemorrhage in 5 of the 6 cases. One of the patients had a return of bleeding after three months.

The results of previous experimental observations coincided with the data obtained in the present study, namely, that relatively small doses of estrogen greatly depressed or eliminated the function of the seminal vesicles while the prostatic secretion, which predominated in the ejaculate, persisted, hence providing a measurable ejaculate.

The decreased volume of semen returned to normal after the administration of estrogen was discontinued, with the important difference that all the blood was absent. The depression of spermatogenesis by the estrogen was not permanent, and in each case spermatozoa of

normal shape appeared in normal numbers some weeks after treatment was discontinued.

Quinland [35] made a study of 33 cases of urinary lithiasis in which the patients were Negroes. The ages of the patients ranged from 8 months to 69 years. Twenty-seven of the patients were males, and 6 were females. The site of the calculi was as follows: kidney in 13 cases, ureter in 4 cases, bladder in 15 cases and prostate gland in 1 case. The size of the calculi varied from renal sand to a large vesical calculus, which weighed 240 Gm. A ureteral calculus which measured 3.8 by 1.8 cm. was removed surgically, and the patient recovered. The causes of death in these cases were not wholly due to resultant complications, such as pyonephrosis, cystitis, peritonitis and septicemia, but to preexisting diseases, such as carcinoma of the prostate, cardiorenal disease, hypertension with terminal apoplexy, bronchopneumonia, tuberculosis and diabetes mellitus. One patient died suddenly, presumably of embolism, seventeen days after operation.

ANTISPASMODICS

Prince and Richardson [36] used a new synthetic antispasmodic, AP-43 (3-[beta diethyl aminoethyl]-3-phenyl-2-benzofuranone hydrochloride) in a series of 61 cases in which spasm of the smooth muscle of the urinary tract was thought to be the major cause of pain. This drug has been found to be extremely effective in relieving pain resulting from ureteral catheterization and retrograde pyelography, and it aids in the passage of a substantial number of ureteral calculi when their size is not such as to preclude their spontaneous passage. In the same type of calculus, AP-43 will relieve pain in the great majority of cases. Apparently, unless the calculus causes pain, the drug is not effective in assisting the passage of the stone.

In 13 of 19 cases of severe vesical spasm, complete relief was obtained. It was suggested that AP-43 is of value when used in the following circumstances: prior to retrograde pyelography, to prevent postpyelogram pain; prior to cystoscopy, as an aid to ureteral catheterization, and prior to cystoscopic manipulation of ureteral calculi, to produce greater relaxation of the ureter.

Undesired side effects are uncommon and usually mild in nature when seen; there was no evidence of cumulative toxic effects in this series of cases. The drug may be given effectively either by mouth or intramuscularly. The trade name "Amethone" has been tentatively accepted for AP-43.

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35. Quinland, W. S.: Urinary Lithiasis: Review of Thirty-Three Cases in Negroes, J. Urol. **53**:791-804 (June) 1945.

36. Prince, C. L., and Richardson, E. J., Jr.: AP-43: A New Antispasmodic for Use in Urology, J. Urol. **54**:75-86 (July) 1945.

SYPHILIS AND FERTILITY

Michelson [37] studied the fertility of 50 men who had syphilis. The characteristics of the semen, particularly of the spermatozoa, were employed in judging the degree of fertility in each case. A similar study of 50 nonsyphilitic men was made and the results compared with those in the cases of syphilis. It is evident that the fertility of this particular group of syphilitic men was equal to and compared favorably with that of the 50 nonsyphilitic men. It would appear that syphilis when correctly treated rarely affects the fertility of man.

37. Michelson, L.: A Study of Syphilis in the Male Relative to Fertility, J. Urol. **53**:808-811 (June) 1945.